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Prevalence and severity of asthma, rhinoconjunctivitis and eczema in children from the Bangkok area: The Global Asthma Network (GAN) Phase I

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Abstract

Background: As noted in the reports of ISAAC phase I and III, allergic diseases are very common in Thailand, especially among younger children.

Objective: The objectives of this project are to study the prevalence and severity of the most common allergic diseases. i.e. asthma, rhinoconjunctivitis and eczema among children living in Bangkok.

Methods: A cross-sectional multi-centers survey using GAN Core questionnaires on asthma, rhinoconjunctivitis and eczema symptoms were completed by parents of children aged 6–7 years and children aged 13–14 years.

Results: The total of 6,291 questionnaires were eligible for the analysis. The cumulative vs. 12-month period prevalence of the three conditions for all children were: 24.4% vs. 13.5% for wheezing, 51.1% vs. 43.6% for rhinitis and 15.8% vs. 14.2% for eczema, respectively. The period prevalence of wheezing for younger children (14.6%) was higher than for older children (12.5%). Prevalences of severe wheeze and exercise wheeze were more common among older children (2.9% and 14.8%). The 12-month prevalences of rhinitis (43.6%) and rhinoconjunctivitis (16.3%) were higher in both age groups. Eczema, as the same to the other conditions, occurred more frequently in both groups (period prevalence of 14.3% and 14.0%) comparing to ISAAC phase III.

Conclusion: Allergic conditions are very common diseases among children residing in Bangkok. There is an urgent need for an in-depth study to define epidemiological factors responsible for this increase.

Key words Asthma, rhinoconjunctivitis, eczema, ISAAC, GAN

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Introduction

Allergic diseases are among the most common chronic diseases in children and adolescents leading to a substantial health and socioeconomic burden. The International Study of Asthma and Allergy in Childhood (ISAAC) phase I and III surveys reported an overall increase in the prevalence of eczema and allergic rhinoconjunctivitis worldwide. However, no changes in the prevalence of asthma among 13-14-year-old children over a mean period of 7 years was observed.[1-3]

The ISAAC phase I study in Thailand was conducted in 1995-1999 in 3 cities namely; Bangkok,[4] Chiang Mai[5] and Khon Kaen.[6] In Bangkok, the prevalences of three conditions were: asthma 18.3%, rhinitis 44.2% and eczema 15.4%. The ISAAC

phase III studying in Bangkok shown that there is a trend of increasing prevalence of all atopic diseases among children.[7]

The Global Asthma Network (GAN), established in 2012, was formed by scientists from the International Study of Asthma and Allergies in Childhood (ISAAC) 1991–2012 (phases I,[8-13] II[14] and III[1-3,15]) and from the International Union Against Tuberculosis and Lung Disease (The Union[16-19]) following production of the first Global Asthma Report (GAR) 2011,[20] launched in New York (NY, USA) in 2011 at the time of the United Nations high-level meeting on non-communicable diseases. GAN phase I, builds on the ISAAC findings by collecting further information on asthma, rhinitis and eczema, prevalence, severity, diagnoses, asthma emergency room visits, hospital admissions, management and the use of asthma essential medicines.

The objectives of our project are to study the prevalence and severity of the most common allergic diseases. i.e. asthma, rhinoconjunctivitis and eczema in children living in Bangkok. We, herein, report the results of our GAN phase I study in 6,291 children from the two age groups living in the Bangkok area

Methods

Study Design

This study is a cross-sectional, multi-center, study design.

Participants

Seven primary schools and six secondary schools in Bangkok were randomly mapped, stratified and had chosen to represent the population of the entire Bangkok Metropolitan area. In addition, equal numbers of governmental and private schools were selected to avoid an over representation of any predominant socioeconomic classes. Subjects were selected in the same manner as ISAAC phase III. The same age groups were used: 13-14 years old adolescents (self-completed questionnaires) and 6-7 years old children (parental completed questionnaires) and GAN phase I adds their parents as an adult group. Students of both age groups were selected either by grade/level/year or by age group. The questionnaires were sent out to 6,824 children (3,544 for 6-7 years and 3,280 for 13-14 years). Although participation rates for both age groups from these schools were exceptionally high (92.18%), many questionnaires were incompletely answered and were therefore excluded from the analysis. This left a grand total of 6,291 children (3,074 for 6-7 years and 3,217 for 13-14 years) for the inclusion of the analysis. The study was approved by the Human Research Ethics Committee of Thammasat University (054/2560) and the Human Research Ethics Committee of Bhumibol Adulyadej Hospital. The clinical trial number was MTU-EC-ES-4-013/60. Inform consents/assents were obtained by children and by the parents.

GAN Core Questionnaires

GAN Standardized Written Core Questionnaires developed from ISAAC Questionnaires for use in phases I and III, were used in GAN. Demographic questionnaires includes the participant's name, age, date of birth, school (for the adolescents and children), sex and date of interview. Questionnaires were coded by using a unique number for each center, school and participant to ensure confidentiality and to link the questionnaires between the adults, adolescents and children.[21] The written core questionnaires, that was used in ISAAC, have had a question about doctor-diagnosis about asthma, rhinitis and eczema. The core questions were both sensitive and specific, had good content, constructive and concurrent and predictive validity.[22] As in ISAAC, a video of asthma questionnaires was an optional tool: the international version that is being used in ISAAC.[23] This 6-minute non-verbal video showed the clinical signs of asthma symptoms and was developed by the Wellington Asthma Research Group, in order to avoid the problems of translation and understanding of terms of "wheeze" or "whistling" and their uses in culturally heterogeneous population.[24] The video has the advantage of obtaining data from many students quickly and efficiently. The questionnaires were translated into Thai and back translated by a three linguistic proficient individuals and were reviewed and approved by the investigators.

Sample Size

As in ISAAC, a sample size of 3,000 participants per age group (and therefore potentially 6,000 adults of each group) was used. The sample size provided greater than 99% ability (at the 1% level of significance) to detect differences in the prevalence of wheezing of 30% in one center and 25% in another center.[22] As sampling was done by schools, and the information gained from the school pupils and adults, is likely to be a cluster effect. Like ISAAC, the analysis incorporated adjustments in cluster sampling using the design effect,[25] which is important for large studies where clusters of different sizes may be used in different regions. High participation is sought for GAN phase I: at least 80% for 13-14 years old and 70% for 6-7 years old and 70% for adults/parents.

Data Collection and Analysis

Data were collected from July 2017 up to February 2018. Information on the questionnaires was entered in the GAN Epi-Info data entry packaged by GAN Global Center in Auckland, New Zealand (info@globalasthmanetwork.org). Such data were analyzed by using STATA version 14 and expressed in the prevalence of three diseases in both the younger and older groups, separately.

Results

Positive response to wheezing modules for younger and older age groups as well as for all children surveyed are tabulated in **Table 1**. All participants are Thai. The prevalence of ever-wheeze in the younger age group was slightly higher than in the older age group (26.0% vs. 22.9%, $p = 0.004$). This was also true for percentage of current wheeze or wheeze in the past 12 months (14.6% vs. 12.5%, $p = 0.016$) and for attacks within the past 12 months (14.4% vs. 12.6%, $p = 0.029$). Percentages for severe wheeze (1.9% vs. 2.9%, $p = 0.019$) and exercise wheeze (3.0% vs. 14.8%, $p < 0.001$) were much higher among older children. Percentages of night awakening were slightly higher among the younger age group (6.7% vs. 4.2%, $p < 0.001$). Percentages of night cough were noticeably high in both groups (24.2% and 29.9%, $p < 0.001$). The prevalence for diagnosed asthma (asthma-ever, 6.1% and 8.8%, $p < 0.001$) were much lower than wheezing-ever for both groups (26.0% and 22.9%).

Table 1. Percent of positive response of questions in wheezing module.

Symptoms	All (n = 6,291) (95%CI)	6-7 years (n = 3,074) (95%CI)	13-14 years (n = 3,217) (95%CI)	P Value
Current wheeze	13.5 (12.7, 14.3)	14.6 (13.4, 15.9)	12.5 (11.4, 13.7)	0.016
Wheezing ever	24.4 (23.4, 25.5)	26.0 (24.5, 27.6)	22.9 (21.5, 24.4)	0.004
Asthma ever	7.4 (6.8, 8.1)	6.1 (5.2, 6.9)	8.8 (7.8, 9.7)	< 0.001
Symptoms in past 12 months				
- attacks	13.5 (12.6, 14.3)	14.4 (13.2, 15.7)	12.6 (11.4, 13.7)	0.029
- night waking	5.4 (4.9, 6.0)	6.7 (5.8, 7.6)	4.2 (3.5, 4.9)	< 0.001
- severe wheeze	2.4 (2.0, 2.8)	1.9 (1.5, 2.4)	2.9 (2.3, 3.4)	0.019
- exercise wheeze	9.0 (8.3, 9.8)	3.0 (2.4, 3.6)	14.8 (13.6, 16.0)	< 0.001
- night cough	27.1 (26.0, 28.2)	24.2 (22.7, 25.7)	29.9 (28.3, 31.5)	< 0.001

Current wheeze: wheeze in the past 12 months
Symptoms of severe asthma: respondents with current wheeze who had > 4 attacks of wheeze in the last year or had > 1 nights per week sleep disturbance from wheeze in the last year or had wheeze affecting speech in the last year.
P Value for Chi square test of positive response symptom between age groups

Table 2. Percent of positive response to video questionnaires for wheezing

Description of video sequences:	13-14 years (n = 3,217)	
	Cumulative (95%CI)	12 month Prevalence (95%CI)
Wheezing at rest	11.9 (10.8, 13.1)	8.9 (7.9, 9.9)
Exercise wheeze	13.5 (12.3, 14.5)	9.0 (8.1, 10.0)
Night wheeze	6.6 (5.8, 7.5)	5.6 (4.8, 6.4)
Night cough	23.4 (21.9, 24.8)	17.9 (16.6, 19.3)
Severe wheeze	8.1 (7.2, 9.1)	5.8 (5.0, 6.6)

Current wheeze: wheeze in the past 12 months

Table 3. Percent of positive response of questions in rhinitis modules.

Symptoms	All (n = 6,291) (95%CI)	6-7 years (n = 3,074) (95%CI)	13-14 years (n = 3,217) (95%CI)	P Value
Current rhinoconjunctivitis or Current AR	16.3 (15.4, 17.2)	15 (13.8, 16.3)	17.5 (16.2, 18.8)	< 0.001
Current nose symptom	43.6 (42.4, 44.8)	38.2 (36.5, 39.9)	48.8 (47.0, 50.5)	< 0.001
Current eye symptom	16.6 (15.6, 17.5)	15.0 (13.8, 16.3)	18.0 (16.7, 19.4)	0.001
Nose ever	51.1 (49.9, 52.4)	47.3 (45.5, 49.0)	54.9 (53.1, 56.6)	< 0.001
Hay fever ever	27.4 (26.3, 28.5)	24.5 (23.0, 26.0)	30.1 (28.5, 31.7)	< 0.001
Severe rhinoconjunctivitis	1.5 (1.2, 1.7)	1.0 (0.6, 1.3)	1.9 (1.4, 2.4)	< 0.001

Current rhinoconjunctivitis or Current AR: Current nose symptom and current eye symptom
Severe rhinoconjunctivitis: Current rhinoconjunctivitis and answer A LOT to question " In the past 12 months, how much did this nose problem interfere with your (child) daily activities?
P Value for Chi square test of positive response symptom between age groups

As for male: female ratio, there was no predominance for males over females other than responses for question of 'asthma ever' (1.36).

The self-reported video questionnaires completing by the 13-14-year-old group revealed a cumulative vs. current prevalence of: wheezing at rest (11.9% vs. 8.9%), exercise wheeze (13.5% vs. 9.0%), night wheeze (6.6% vs. 5.6%), night cough (23.4% vs. 17.9%) and severe wheeze (8.1% vs. 5.8%) (**Table 2**). Percentages for night wheeze (5.6%) was slightly higher than that derived from the written questionnaires (4.2%). The video responses to exercise question (9.0%) was lower than that from the written ones (14.8%). The prevalence of severe wheeze from video responses was 5.8%, which is twice of the written questionnaire (2.9%).

In **Table 3**, prevalences of rhinitis and other associated symptoms are shown. An exceptionally high number of children from both age groups (47.3% and 54.9%) reported nasal symptoms. Approximately 43.6% experienced nasal symptoms

Table 4. Percent of positive response of questions in eczema module.

Symptoms	All (n = 6,291) (95%CI)	6-7 years (n = 3,074) (95%CI)	13-14 years (n = 3,217) (95%CI)	P Value
Rash ever	15.8 (14.9, 16.7)	16.3 (15.0, 17.6)	15.2 (14.0, 16.5)	< 0.001
Eczema ever	22.8 (21.8, 23.9)	28.6 (27.0, 30.2)	17.3 (16.0, 18.7)	< 0.001
Flexural area	10.8 (10.1, 11.6)	11.7 (10.6, 12.9)	10.0 (8.9, 11.0)	0.024
Symptoms in past 12 months				
- rash	14.2 (13.3, 15.0)	14.3 (13.1, 15.6)	14.0 (12.8, 15.2)	0.684
- rash clear	9.6 (8.9, 10.3)	9.1 (8.1, 10.2)	10.0 (9.0, 11.1)	0.226
- night waking	4.7 (4.2, 5.2)	5.6 (4.8, 6.4)	3.8 (3.2, 4.5)	0.001

Severe eczema: Current eczema associated with sleep disturbance 1 or more nights per week
P Value for Chi square test of positive response symptom between age groups

within the past 12 months: whereas, 16.6% reported from concomitant eye symptoms. These children indicated that their symptoms were bothersome at some point. The prevalence of current AR (current rhinoconjunctivitis) of both age group (15% vs. 17.5%). The prevalence of severe AR in children aged 6-7 years and 13-14 years were 1.0% and 1.9% respectively. The prevalence of severe AR in all children was 1.5%. Although the term 'hay fever' does not exist in the Thai language, 27.4% indicated that they suffered from 'allergy to the air', a common term denoting hay fever in Thai.

Positive responses to questions in the eczema module are shown in **Table 4**. The percentage of younger children reported 'rashes within the past 12 months' was 14.3% and up to 11.7% indicated rashes localized in areas typical diagnosis of atopic dermatitis. Slightly lower numbers were reported in older children (14.0% and 10.0%). Many children with a rash indication had mostly cleared within the past twelve months (9.1% and 10.0%). and was not bothersome to them. The prevalence of severe eczema in children aged 6-7 years and 13-14 years were 5.6% and 3.8% respectively. The prevalence of severe eczema in all children was 4.7%. It can be suggested that the degree of eczema was mild among Thai children. Male to female ratio suggested that slightly more females than males were affected with these rashes.

In our study, there were strong associations with other allergic diseases: in asthma patients: 32.5% had AR and 21.8% had eczema, AR patients: 27.1% had asthma and 24.6% had eczema, eczema patients: 37.1% had asthma and 27.4% had AR.

Discussion

As noted in the reports of ISAAC phase I and III, asthma was very common in Thailand, especially among younger children.[4,7] In this study, prevalence rates of current wheeze based on the written questionnaire in the 6–7 years is similar to the prevalence in the ISAAC study phase III; in Bangkok[7] (14.6% vs. 15.0%, p = 0.541). Meanwhile, the prevalence rate in the 13–14 years age group is slightly lower than prevalence in the ISAAC study phase III; in Bangkok[7] (12.5% vs. 13.9%, p = 0.024). Slightly higher than the ISAAC phase III: the mean global prevalence for current wheeze (11.5% and 4.9%) and the Asia -pacific prevalence (9.5% and 8.8%).[9]

The cumulative prevalence of wheezing based on the video questionnaires from this study (11.9%) is closed to the prevalence of the ISAAC study phase III from Bangkok (11.5%).[7] This is much higher than the Asia-Pacific prevalence (5.5%) and, also the global prevalence (8.7%) of the ISAAC study phase III.[9] The prevalence of severe asthma (written questionnaires) in the 13-14 years age group is 2.9%. This is lower than the prevalence of severe asthma from the ISAAC study phase III: globally (6.9%) ranging from 3.8% in Asia-Pacific, Northern and Eastern Europe to 11.3% in North America (compared to Bangkok 4.0%).[9]

The Asthma Insight and Management (AIM) survey (2011) reported the asthma exacerbations in the past 12 months: Thailand (36%), South Korea (47%), Australia (54%), and China (67%).[26] Thai patients that uses controller medication is 54% in previous month. Pill controller medication is the most common form among those reporting controller medication used (67%), whereas 57% reported taking an inhaler.[27]

The new GAN phase I survey, however, portrayed a differing epidemiological outlook than from what has been felt among practitioner caring for asthmatic patients. These preliminary data have shown that prevalence of asthma in younger and older children is still over 10% of the population surveyed. Moreover, the prevalence for those with severe wheeze is roughly 2%. The Chest and Allergy Societies in Thailand have regularly updated asthma guidelines for adults and children. Besides, social media has made it easier for parents/patients to find appropriate professional care. An increase in the availability of asthma controllers throughout the country may help lessen the severe asthma attacks presented to emergency rooms and requiring hospital admissions in this country. Among these drugs, inhaled steroids are very popular. Since generic versions of these controllers are cheaper than original version, they were included in Essential Drug List subsidized by the Government for those eligible for medical supports (governmental employees, those under the social security program and universal health coverage). Effective advocacy by non-governmental organizations, smoking in homes and public places is now rare event. Thailand has enforced stricter regulations to reduce outdoor air pollution, such as cleaner air emissions and vehicle fuels.

Ecological economic analyses also revealed that although the high-income centers tended to have a higher prevalence of current wheeze, a reverse trend was found in the prevalence of symptoms of severe asthma among current wheezers. There may be several reasons underlying this observation. First, asthma care is likely to be poorer in these developing countries, although a recent epidemiological survey showed that suboptimal

asthma management was a global phenomenon.[28,29] Secondly, there may be less awareness of wheeze being a symptom of asthma, even in those with frequent wheezing, similar to the situation amongst ethnic minorities in developed countries.[30] This notion is further supported by the finding that undiagnosed asthma among those current wheezers with severe asthma symptoms was most commonly seen in these lower income countries. Children with undiagnosed frequent symptoms are also more likely to receive inadequate care for their asthma and may fall into a vicious downward spiral of asthma control.[30] Thirdly, differences in the levels of environmental exposure, including air pollutants and infective agents, may also contribute to the greater severity observed in these countries.

GAN phase I has provided the most comprehensive estimate of the worldwide symptom prevalence of asthma to date. This global map of asthma is invaluable not only for public health planning, but also for generating hypotheses in explaining the etiological factors for this common disorder.

In our study, the prevalence of current AR or current rhinoconjunctivitis in the 6–7 year and 13–14-year age groups are 15.0%, 17.5% respectively. As the ISAAC study phase III, the prevalence of current AR of Thai children from the Bangkok area were 13.4% and 23.9% respectively.[7] It is slightly higher than the mean of global prevalence (9.1%, 16%), and the Asia -Pacific prevalence (5.8% and 14.5%).[10]

In our study, the prevalence of current eczema symptoms in the 6–7 years and 13–14 years age groups are 14.3%, 14.0% respectively. These values are slightly higher than those from the ISAAC study phase III study in Bangkok (13.3% and 10.4%).[7] However, our GAN results on eczema is much higher than the ISAAC study phase III study elsewhere: the mean global prevalence (7.9%, 7.3%) and the Asia-pacific prevalence (4.7% and 5.3%).[12]

For developing countries, Thailand has been noted to has an increased in the number of patients with food allergy and atopic dermatitis. The reason for this worrisome and unusual increase is uncertain at this point. Similarly, results of GAN phase I survey substantiate the increasing numbers of children in both age groups. If a phenomenon of allergic march operates in this part of the world, one should witness an increase in the number of asthmatic patients rather than a decrease in the next decade.

Strengths and Weaknesses of the Study

The major strengths of our study included a standardized written core questionnaires (GAN 2016) developed from ISAAC Questionnaires, well-established standardized protocol and high response rate. The establishment of GAN 2016 questionnaires allows an excellent opportunity for different countries to establish their own basic epidemiological data for allergic diseases that can be compared internationally. A video asthma questionnaire (6-min non-verbal video) shows clinical signs of asthma symptoms to avoid problems of translation and comprehension of terms such as "wheeze" or "whistling" and their use in culturally heterogeneous population. One limitation of our study is that symptoms of allergic rhinitis were self-reported in the questionnaire, therefore, we could not confirm with physical examination and laboratory investigations.

In conclusion, the result of GAN phase I in Bangkok showed a slightly increase of prevalence of eczema in both age groups, while prevalences of asthma and allergic rhinitis have become stabilized in both age groups. Most Thai children with asthma had coexisting rhinitis, and a portion of patients with rhinitis also had asthma. Allergic conditions are very common among children residing in Bangkok. There is an urgent need for an in-depth study to define epidemiological factors responsible for this increase.

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