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SPECIAL ARTICLE

Epidemiology and Current Status of Allergic Rhinitis and Asthma in Thailand-ARIA Asia-Pacific Workshop Report

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SUMMARY The allergic diseases of the airway, *i.e.* allergic rhinitis and asthma, are on the increase in Thailand and their prevalence shows no signs of abating. When compared with a previous study, the incidence of wheezing had increased 4 fold (from 4.2% to 18.3%), and allergic rhinitis increased nearly 3 fold (from 17.9% to 44.2%). The results of the ISAAC phase III study revealed that the frequency of allergic diseases of the respiratory tract increased significantly from the ISAAC phase I survey performed in 1995; *i.e*. asthma increased from 12.2% to 14.5%, and allergic rhinitis from 37.9% to 50.6%. Allergic rhinitis exerts a major impact on the quality of life of Thai patients.

The results of skin prick testing have indicated the leading causes of indoor (house-dust mites, house dust, cockroaches, dogs and cats) and outdoor pollen (Bermuda grass, para grass, sedge, careless weed) allergens. Molds (represented by *Cladosporium*), although prominent in an aeroallergen survey, returned a low percentage of positive skin prick reactions, and therefore, were considered low in allergenicity.

In Thailand, there are clinical practice guidelines for both allergic rhinitis and asthma which are comparable to the international guidelines like ARIA and GINA. Sufficient kinds of pharmacotherapy are on the National List of Essential Drugs. Yet due to the limited number of trained allergists, many patients are seen by general physicians, and often, the appropriate diagnostic tests and treatments are not provided. In addition, the financial burden for quality health care may be prohibitive for those without private health insurance in spite of the implementation of a universal health care system for all Thai citizens, which is less than optimal.

Although allergic rhinitis (AR), seems to be a trivial disease, it has been proven to be a major health problem with more than 600 million patients suffering worldwide.[1-4] Therefore, a group of WHO experts met at the ARIA (Allergic Rhinitis and Its Impact on Asthma) workshop in 1999 to extensively review the literature and produce an evidence-based document which is a state-of-the-art guideline on the diagnosis and treatment of AR, for specialists as well as general practitioners (GP) and other health care professionals.[5] It is intended to be a standard of care of AR worldwide. The ARIA WHO document was subsequently updated and published in 2008.[6]

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An important aspect of the ARIA document is the highlighting of the interactions between allergies of the upper and the lower airways focusing on epidemiology, diagnosis, management and prevention. A new classification of allergic rhinitis and its severity has also been proposed. Unfortunately, this ARIA WHO document was produced by a group of WHO experts that did not include representatives from most of the Asian countries. In addition, the relevant data from developing countries, which are usually not published in international journals, were neither reviewed nor included in their considerations. In particular, in the case of Thailand, it is doubtful whether the recommendations from the ARIA guidelines are applicable to the characteristics of the average Thai AR patient, the current practice and situation of the health care system in Thailand.

Therefore, the purpose of this paper is to provide a review of the epidemiological data of AR and the status of asthma in Thailand with special attention to their routine management and the incumbent socioeconomic burden.

Epidemiology

The prevalence of allergic diseases in Thailand was initially studied in 1975 using a questionnaire survey in university students developed by Tuchinda[7] and indicated that the frequency of AR and asthma was 23.6% and 2.4%, respectively. In 1997, Bunnag *et al*.[8] also surveyed university students and found that the prevalence of AR decreased to 21.9% while the incidence of asthma increased to 4.8%. After the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was launched in 1991, Vichyanond *et al*.[9] in 2002 administered this international standardized phase I protocol to 3,631 university students from six universities in Bangkok. It was found that the prevalence of rhinitis within the past 12 months was 61.9% but AR students who had nasal and eye symptoms together within the past 12 months had an incidence rate of 26.3%. On the other hand, the prevalence of wheeze within the past 12 months and the diagnosis of asthma in this survey were 10.1% and 8.8%, respectively.

In a 1998 epidemiological survey[10] of allergic diseases in metropolitan Bangkok, the ISAAC phase I questionnaire was administered to 7,341 children dichotomized into two age groups, 6-7 years (3,628) and 13-14 years (3,713). The cumulative (ever had rhinitis) and 12 month prevalence (symptom within the past 12 months) of rhinitis for all subjects was 44.2% and 38.7%, respectively, while that for wheezing was 18.3% and 12.7%, respectively. Wheezing over the 12 month period in the older children (13.6%) was higher than that for the younger group (11.7%). In children who had both nasal and eye symptoms, the cumulative and 12 month period prevalence rate was 30.3% and 13.1% in that order.

In the ISAAC questionnaire, it was suggested that subjects who had a combination of nasal and eye symptoms were more likely to have AR. However, data from the ENT Allergy Clinic, Siriraj Hospital, revealed that among 1,394 patients who were confirmed by positive skin prick testing to have perennial AR, only 54.5% complained of eye symptoms (Bunnag *et al.,* unpublished data). This suggests that the correlation between AR and eye/nasal symptoms is less than perfect. Similar surveys using the ISAAC phase I questionnaire were also undertaken in Chiang Mai, the northern province of Thailand,[11] and in Khon Kaen, the north-eastern province.[12] The frequency of AR and asthma in children of both age groups in those two centers were similar to the Bangkok study.[10] When the findings from the 2002 ISAAC phase I study[9] were compared with a previous 1990 survey of allergic diseases in Thai children,[13] the prevalence of AR had increased nearly 3 fold (from 17.9% to 44.2%) and the period prevalence of wheezing had also increased more than 4 fold (from 4.2% to 18.3%). Even though ISAAC was launched one year before the 1990 study, the results indicated a significant increase in asthma-related symptoms in Thai children.

In order to examine time trends in the prevalence of atopic diseases in children, the ISAAC phase III study was performed in 2001 in 2 cities: Bangkok and Chiang Mai. The data revealed that the prevalence of rhinitis and rhinoconjunctivitis among both age groups increased in both centers as compared to the ISAAC phase I study in 1995. However, the frequency of asthma increased only in the 6-7 year age group while it stabilized in the 13-14 year age group in Bangkok, and actually decreased

in Chiang Mai.[14] It was postulated that recent environmental changes may have deleteriously affected the younger children[1] while the advent of puberty in the older children may have exerted a protective influence.

At present, only one study[15] has evaluated the incidence of AR in the general population spanning all age groups (3,124 subjects) living in Bangkok and its vicinity. An in-house survey-type questionnaire was specifically developed for this purpose. The cumulative prevalence of chronic rhinitis was 13.15% which, in general, is less than that observed in university students.

Comorbidity of rhinitis and asthma

The united airways disease hypothesis[16] suggests that disorders affecting the upper airways producing nasal inflammation are likely to affect the lower airways resulting in bronchial inflammatory responses. This comorbidity between AR and asthma was observed by Trakultivakorn *et al*.[14] who found that 55-75% of asthmatic children had AR while 13.9-25% of rhinitis children had asthma. These results are similar to clinical studies indicating that 80-100% of patients with asthma have rhinitis and conversely, 50% of patients with rhinitis have asthma, and to the findings in the AR patients treated at the ENT Allergy Clinic at Siriraj Hospital, Bangkok, that 16.1% had concomitant asthma (Bunnag *et al*., unpublished data).

Classification of AR according to seasonal variation

The tropical climate of Thailand consists of 3 seasons, summer (from March to June), the rainy season (from July to October) and winter (from November to February). However, what is called winter in Thailand is not the same as in the Western hemisphere. The lowest temperature in the winter in Bangkok rarely drops below 15°C, even in the northern plains of Thailand. However, in the mountainous north, at elevation, the temperature occasionally approaches 0°C. Therefore, pollens never completely disappear from Thailand's climate. According to previous aeroallergen surveys in Thailand,[18-20] pollens are present all year round with the greatest frequency observed during the winter months. Grass and weed pollens e.g. Bermuda grass (*Cynodon dactylon*), para grass(*Panicum purpurascens*), sedge (*Carex species*) and careless weed (*Amaranthus hybridus*), are more commonly found in Bangkok than tree pollens. Mold spores are more consistently present throughout the year. The prevalence and types of airborne fungi recovered from the exposed plates in the bedroom and outside the house were only slightly different; i.e. yeast, *Aspergillus*, *Cladosporium* and non-sporulated white fungi had a frequency of occurrence over 50%.[21,22] It is noteworthy that fern spores (*Acrostichum aureum*) were found to be the third most common of airborne particulates in Bangkok having the potential for allergenic reactions.[23]

A survey is recommended to obtain data of the common aeroallergens which may be different in each locality. Moreover, surveillance studies are necessary to detect the seasonal and chronological changes in order to select the relevant allergens for testing and immunotherapy. In highly developed countries, data from daily air sampling (a pollen calendar) are provided to the public which is very convenient and useful for management of allergic patients. Unfortunately, such data are currently not available in Thailand.

It should be mentioned that an AR classification scheme based solely on seasonal and perennial changes may not be relevant in so far as airborne pollens/spores/fungi are continuously present throughout the year in Thailand. Therefore, when the new classification of AR was proposed by the ARIA WHO experts in 2001, the ENT Allergy Clinic quickly adopted this new system and applied it to 365 consecutive AR patients. It is based on two dimensions, i.e. severity (mild, moderate or severe) and longevity (intermittent or persistent) of the illness. Seventy-one percent of the ENT patients had persistent symptoms while 29% were labeled as intermittent. Moreover, 15.3% of the persistent patients had mild symptoms while 84.7% were categorized as moderate to severe. Of those classified as intermittent patients, 39.8% were mild with the remainder (60.2%) exhibiting moderate to severe symptoms (Bunnag C, *et al*., unpublished data). This classification is now used as a guide to the stepwise approach in the pharmacotherapy for AR patients.

Common causative allergens in AR

The percentage of positive skin prick test reactions (wheal and flare ≥ 3 mm) among 736 patients attending the ENT Allergy Clinic at Siriraj Hospital between 2002 and 2004 revealed that house-dust mite is the most common causative allergens (64.7%) followed by house dust (64%), Bermuda grass (52.3%), cockroach (49.8%), para grass (49.4%), sedge (45.9%), careless weed (45.4%), dog (44.2%), cat (39.3%) and *Cladosporium* (38%) respectively.

The indoor allergens obtained from house-dust mites (*Dermatophagoides pteronyssinus, Dp*), house dust, cockroachs (*Periplaneta americana,* Pa), dogs and cats returned an average percentage of 52.4 of positive skin prick test reactions while the mean outdoor allergen percentage from skin-prick testing was 48.25. These data indicate the importance of both types of allergens in the etiology of AR. The fungi as represented by *Cladosporium* and are considered to be both indoor and outdoor allergens, showed the least positive skin test reactions although they were more frequently encountered in the aeroallergen survey than pollens. This designates their low allergenicity.

Impact on quality of life

The SF-36 questionnaire (Thai version)[24] was used to evaluate the quality of life (QOL) of Thai AR patients compared to healthy subjects.[25] The results showed that AR patients had significantly impaired QOL scores than healthy persons in all aspects except the social functioning dimension. When the SF-36 scores of 559 AR patients were compared with 155 hypertensive patients, it was found that AR patients had significantly poorer QOL ratings than the hypertensive patients in four of the eight dimensions (i.e. General health, Vitality, Social functioning and Mental Health). This was an unexpected result because it had been generally accepted that hypertension was a more serious disease than AR. This finding, however, is similar to the study reported by Derebery and Berliner[26] using the SF-36 questionnaire to compare the QOL of allergic patients with five other medical conditions (i.e. hypertension, congestive heart failure, diabetes Type II, recent acute myocardial infarction and clinical depression.)

Moreover, a reliable and validated disease-specific questionnaire[27] was developed for use in Thai AR patients with or without conjunctivitis. This questionnaire, called Rcq-36, consisted of 36 items in 6 dimensions and two independent items (i.e. symptoms 17 items, physical functioning 3 items, role limitations 3 items, sleep 3 items, social functioning 3 items, emotion 5 items, general health 1 item, and absenteeism 1 item). When the SF-36 and the Rcq-36 questionnaires were used to assess the QOL of AR patients and healthy persons, the results showed that both types of health-related QOL questionnaires could demonstrate differences in QOL scores between healthy persons and among patients in different severity subgroups. However, the Rcq-36 questionnaire had a higher correlation with the symptom scores than the SF-36 questionnaire and also included information on sleep and productivity.[28]

Management of AR

In the previously mentioned survey[15] of the prevalence of chronic rhinitis in the general Thai population, among 383 chronic rhinitis subjects, only 10.6% of them had prior allergy skin testing and 3.9% received injection immunotherapy. In this study, 91.3% reported that antihistamines were the most effective and commonly used medication, while 8.3% preferred the use of nasal sprays. These observations may be compared with recent (2007) data from a private rhinology and allergy clinic in Bangkok. Among 200 medically refractory patients with moderate to severe AR symptoms, 27% of them had prior allergy skin testing, 100% were on antihistamines, 32.5% had taken nasal steroids and 12.5% had received allergen immunotherapy (Perapun Rhinology and Allergy Clinic, unpublished observations). Although the data between these two periods showed an increasing percentage of patients receiving allergy skin testing and immunotherapy, it should be noted that the patients in the latter group are patients who can afford the best medical care. Consequently, their data may not be generalizable to all of Thailand.

These observations raise important issues regarding the health care system in Thailand. Generally speaking, the cost of health care is covered (or not) according to the type of one's work; *e.g.* elected/appointed officials and state enterprise employees receive health care that is paid by the Government. Owners of business companies and their executive members provide/pay for their own private health insurance, while the remainder are covered by the social welfare system. The organizational structure of the social welfare system functions by committee deliberations deciding which investigations and treatments will be financially supported. Unfortunately, government assistance for allergy skin testing and immunotherapy are not covered by the social welfare system, thereby necessitating out-of-pocket expenses for those wishing such treatment.

During the last few years, the Thai government has implemented a policy of equitable universal coverage in health care cost for the entire country. Those Thai citizens who have not yet received coverage by other health insurance systems will be accorded free medical assistance in all government hospitals. The medications allowed for this group of Thais are limited to only those on the National List of Essential Drugs approved by the Ministry of Public Health (as shown in Table 1). It can be seen that some second generation antihistamines, intranasal and inhaled corticosteroids, leukotriene receptor antagonists are on the list. However, the generic or local products, if available, are preferred. The patients who need allergy investigations and /or allergen immunotherapy have to be referred by their general practitioners to the specialists in the tertiary care hospitals.

Socioeconomic burden

The socioeconomic impact of AR and asthma in Thailand has not yet been properly studied. However, the data reported in 2004 from the Index of Medical Specialties indicated that 2,250 million Baht were spent for drugs treating allergic diseases and asthma. This expenditure increased about 10% from the year 2003. It does not include cost of clinic or hospital visits, and other indirect expenses such as loss of work productivity, school absenteeism and restricted daily activity. For example, the average number of days absent from work or school because of AR symptoms as reported by Thai patients in the mild, moderate and severe subgroups were 0.89, 1.57, and 3.68 days per month, respectively.[28] Thus, the indirect cost of AR is substantial and should be considered when the diseases are ranked for the national health promotion program.

In order to comply with international standards of health care especially in the era of hospital accreditation together with documentation on patient's right, clinical practice guidelines (CPG) for the most common diseases were developed by a group of experts in pediatrics and otorhinolaryngology. The CPG management of AR for Thai children was promulgated in 1999[29] while the adult version was released in 2001[30] both with the enthusiastic endorsement of the Royal College of Otorhinolaryngologists of Thailand, the Allergy and Immunology Society of Thailand and the Thai Rhinologic Society.

The CPG for management of asthma in Thailand for children[31] and for adults[32] has also been developed. The inhaled route of administration of medications was a highly recommended and well established treatment modality for asthma in the Thai CPG as well as in the international guidelines. However, the use of inhaled medications for asthma control as revealed by two separate surveys,[33,34] remains less than optimal, which is not surprising since standard asthma treatment remains inadequate even in the United States.[35]

The principles underlying the development of the Thai CPGs are not much different from those developed in Western countries. Most if not all are based on research evidence and the recommendations of experts whose opinions vary little except for slight modifications in local conditions. However, in real life situations, due to the tremendous shortage of well-trained allergists especially in rural areas, coupled with a paucity of health education messages and public awareness, allergy skin testing for definite diagnoses, the use of topical steroids, allergen immunotherapy and allergen avoidance measures are still much under practiced

In conclusion, in order to reach the ARIA WHO goals, the entire range of health care systems for managing AR and asthma in Thailand needs to be reconsidered in several aspects. The allergist training

program must be expanded both in quantity and quality. Health education campaigns must be initiated to increase not only the publics' awareness but also that of patients and physicians. The standard management of allergic diseases must be acknowledged and the costs assumed by all responsible health care providers. And last but not least, the increasing spiral of AR and asthma must be recognized and efforts towards its arrest and prevention must be a central focus of the important health care policy of the nation.

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Appendix 1 Drugs for treating allergic rhinitis and asthma in the Thai National List of Essential Drugs, 2008

Drugs	Formulation
1. Antihistamines	
1.1 Brompheniramine maleate	Tablet and syrup
1.2 Chlorpheniramine maleate	Capsule, tablet and syrup
1.3 Diphenhydramine HCl	Capsule, sterile solution
1.4 Hydroxyzine	Tablet and syrup, 10 mg, 25 mg
1.5 Cetirizine HCl	Tablet and syrup
1.6 Loratadine	Tablet and syrup
2. Oral nasal decongestant	
2.1 Pseudoephedrine HCl	Tablet and syrup
3. Nasal preparation	
3.1 BDP	Nasal spray, 50 mcg, 100 mcg
3.2 Budesonide	Nasal spray
3.3 Fluticasone propionate	Nasal spray
3.4 Triamcinolone acetonide	Nasal spray
3.5 Ephedrine HCl	Nasal drop, 1%, 3%
3.6 Oxymetazoline HCl	Nasal drop/spray, 0.025%, 0.05%
4. Bronchodilator	
- Adrenoceptor agonists	
4.1 Procaterol HCl	Tablet and syrup, 25 mcg, 50 mcg
4.2 Salbutamol sulfate	Tablet, syrup, DPI, MDI, solution for nebulizer, 20 ml
4.3 Terbutaline sulfate	Tablet, syrup, DPI, MDI, solution for nebulizer, 2 ml
- Compound antimuscarinic + bronchodilators	
4.4 Ipratropium bromide + fenoterol hydrobromide	MDI, solution for nebulizer, 2 ml
- Theophylline	
4.5 Aminophylline	Tablet, 100 mg, sterile solution for injection
4.6 Theophylline	SR capsule/tablet, 200 mg
4.7 Theophylline + Glyceryl guaiacolate	Syrup (60 ml)
5. Inhaled corticosteroids	
5.1 BDP	DPI, MDI
5.2 Budesonide	DPI, MDI, suspension for nebulizer
5.3 Budesonide + Formoterol	DPI
5.4 Fluticasone	MDI, suspension for nebulizer
5.5 Salmeterol + Fluticasone	DPI, MDI
6. Leukotriene receptor antagonists	
6.1 Montelukast sodium	Chewable tablet, 5 mg, film-coated tablet 10 mg

BDP, beclomethasone dipropionate; DPI, dry-power inhaler; MDI, metered-dose inhaler; SR, slow-released