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## PATTERN OF SKIN PRICK TEST RESPONSES TO COMMON ALLERGENS IN PATIENTS WITH ALLERGIC RHINITIS IN BRUNEI DARUSSALAM.

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### ABSTRACT

**Background:** Allergic Rhinitis (AR) is a prominent inflammatory disorder of the nasal mucosa caused by exposure to allergens. Skin prick testing (SPT) is a standard method for evaluating the pattern of allergen sensitivity among patients suffering from AR. The objective of this study was to evaluate the sensitivity pattern of common allergens associated with AR in a tertiary care centre in Brunei. **Materials and Methods:** We prospectively recruited 98 patients with a clinical diagnosis of AR to undergo SPT in an outpatient setting. SPT was performed using 14 common allergens; house dust mites, *Blomia tropicalis*, German cockroach, feline dander, wheat flour, peanut, banana, egg white, milk, shrimp, chicken, fish mix, Bermuda grass and pollen with two controls (histamine and saline). **Result:** Mean age of the study group was 33.5±15.5 years and majority were female (73.5%). Nasal obstruction (86%) was the most common symptom reported by patients followed by rhinorrhoea (72%) and nasal itch (72%). Of the 98 patients who underwent SPT, 86.7% had positive SPTs while 13.3% were negative. The most common offending allergens were house dust mite (69.4%), *Blomia tropicalis* (61.2%) and shrimp (36.5%). **Conclusion:** The prevalence of AR is increasing in rapidly developing countries such as Brunei Darussalam. From this study, we found that the house dust mite, *Blomia tropicalis* and shrimp were the most common allergens causing AR. Identifying the common allergens is useful in implementing effective preventative, diagnostic and treatment plans in an effort to help decrease the health burden of this disease in the Bruneian population.

**Keywords:** Allergic rhinitis, skin prick test, food allergens, mites

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## INTRODUCTION

According to the ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines, Allergic rhinitis (AR) is defined clinically as the presence nasal hypersensitivity symptoms induced by an Ig E-mediated inflammatory response after exposure to an offending allergen.<sup>1</sup> It is char-

acterised by symptoms such as sneezing, nasal congestion, nasal discharge (clear and watery), post nasal drip, cough, irritability and fatigue. It is also often accompanied by itching of the eyes, nose and palate.<sup>2</sup> It can be described as either intermittent (<4 days/week or <4 weeks) or persistent (>4 days/week or > 4 weeks) and to be either mild with normal sleep and no impairment of daily activities or moderate/severe with abnormal sleep and impairment of daily activities.<sup>1</sup> AR is the most common type of allergic disease

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seen in the primary care settings, which can be seasonal, occupational or perennial and is the sixth leading cause of morbidity in the world.<sup>3</sup>

In the last two decades the prevalence of AR has increased, especially in the developed western world, with prevalence rate ranging between 10% to 41% in Europe and 11% to 33% in the United States.<sup>2</sup> Asia has a relatively high prevalence of AR with reported prevalence rates in school children ranging from 20-50.6% in ASEAN countries and 32% in Japan.<sup>3,4</sup> Studies have shown the negative impact that AR can have on physical and mental health, its exacerbations on other illnesses such as asthma, rhino-sinusitis, sleep disorders and middle ear disease if not managed properly. Moderate to severe disease has also been shown to decrease performance and productivity in work, school and other social aspects of life, due to the repetitive nose blowing, sleep disturbance and inability to concentrate.<sup>4,5</sup>

AR is still largely under-diagnosed and under-treated in many countries.<sup>6</sup> The British Society for Allergy and Clinical Immunology (BSACI) guidelines for management of allergic and non-allergic rhinitis recommended the routine use of skin prick test (SPT) in all patients presenting with rhinitis symptoms in order to differentiate AR from non-AR.<sup>7</sup> SPT is sensitive and specific as well as cheap and can be easily performed in an outpatient clinic setting.<sup>8</sup> Currently, there are no studies documenting the common allergens causing AR in Brunei Darussalam. Hence the objective of this was to evaluate the pattern of SPT responses to 14 common allergens associated with AR in our local population.

## **MATERIALS AND METHODS**

### **Patients**

This prospective cohort study randomly recruited 98 patients with a positive history of

two or more symptoms of AR such as rhinorrhoea, sneezing, nasal blockage, itchiness of eyes and nose, referred to the Otorhinolaryngology Outpatient clinic at Raja Isteri Pengiran Anak Saleha (RIPAS) hospital. Diagnosis was confirmed and made by an Otorhinolaryngologist. Patients with known atopic dermatitis on their arms and recent exacerbation of asthma and/or acute episode of AR which was not controlled with medications were excluded. This research study was approved by the Medical and Health Research and Ethics Committee of RIPAS Hospital.

A full detailed history and physical examination of the recruited patients were carried out initially in the clinic. Patients were then asked to complete a questionnaire before proceeding with skin prick testing. Written informed consent were obtained prior to SPT.

### **SPTs and reaction measurements**

SPTs were performed using 14 common allergens found in South-east Asian countries (Malaysia, Singapore and Thailand) and two controls were used in the SPT. The common allergens tested were mites (*Blomia Tropicalis*, *Dermatophagoides mix*), wheat flour, bermuda grass, pollen IV, peanut, banana, egg white, milk, shrimp, chicken, German cockroach, cat and fish mix. Histamine and saline were used as the positive and negative controls respectively. All 14 allergens were obtained as standardised test kits from ALK-Abello (ALK-Abello Inc, USA).

All SPTs were performed by author (SN) at the Otorhinolaryngology outpatient clinic according to a Standard Operating Procedure based on previous published methods and technique.<sup>8</sup> A multiple skin test applicator with 8 epidermal needles (Multi-Test II, Lincoln Diagnostics, Inc, USA) were coated with test allergens by dipping in 8 shallow wells containing a small aliquot of the standardised test allergens (ALK-Abello, Inc, USA). The coated applicator was then used to introduce

the allergens into the skin on the ventral part of the forearm, which was cleaned with alcohol gel prior to injection. A second multiple skin test applicator was used for the remaining six allergens and both (positive and negative) controls in separate eight shallow wells.

The allergens will interact with the specific IgE bound to mast cells which causes the degranulation and release of inflammatory mediators from mast cells that stimulate nerves, glands and blood vessels to cause a wheal or flare reaction peaking after about 15 minutes, if the patient is allergic to a particular allergen.<sup>10,11,12</sup> The sites were examined after 20 minutes for presence or absence of wheals or flares. The size of a weal at least 3mm and flare of at least 10mm larger than the negative control was taken as positive reactions. After the SPT, the patients were advised to remain in the clinic for 30 minutes, to observe for any immediate adverse reactions such as urticaria or anaphylaxis.

### Statistical analysis

All data and measurements were collected and entered into an Microsoft excel file which was later used for analysis at the end of the study. All continuous data were presented as mean  $\pm$  standard deviation. Nominal data was presented as percentages.

## RESULTS

Out of the 98 patients with a diagnosis of AR studied, 72 (73.5%) were females and 26 (26.5%) males. The mean age of the group was  $33.5 \pm 15.5$  years (range 8 to 72 years). Thirty (30.6%) patients had positive family history of atopy. Twenty-four (24.5%) patients have previously been diagnosed with asthma, 34 (34.7%) with eczema and skin rashes. A history of food or drug allergies were present in 43 patients.

Majority of patients complained of

nasal congestion (87.7%) as the most common symptom. This was followed by symptoms of rhinorrhoea (73.5%) and nasal itch (73.5%), sneezing (71.4%), itchy eye (56.1%), itchy throat (48%), post-nasal drip (46.9%), facial pain (42.9%), chronic headache (38%) and chronic cough in 15.3% (Table 1). Positive family history of AR was present in 30 patients. Twenty-four patients have a previous diagnosis of asthma.

Eighty-five (86.7%) patients have positive SPT results (Table 2). The remaining 13 (13.3%) patients have negative SPT results, hence their diagnoses were subsequently amended to non-allergic rhinitis for which the treatment is different. Of the 14 common allergens tested, insect/animal were responsible for causing majority cases of AR with positive reaction to house dust mite allergens seen in 69.4% of patients tested (Table 2). This was followed by *Blomia tropicalis* (61.2%), feline dander (22.4%) and German cockroach (21.2%). Among the food allergens, shrimp was positive in 36.5% of patients, followed by wheat flour (17.6%), chicken (14.1%), fish (12.9%), banana (9.4%), milk (8.2%), egg white (5.9%) and peanuts (4.7%). Aero-allergens such as Bermuda grass and pollen were positive in 9.4% and 5.9% of the patients tested respectively, suggesting that seasonal allergic rhinitis is less common in Brunei Darussalam. Only 17 patients had monoallergen tested positive on SPT and 3 patients tested positive for 11 or more allergens on SPT.

## DISCUSSION

There has been an increase in the prevalence of atopy and allergic diseases such as AR around the world, especially in the both developed and rapidly developing countries such as Brunei.<sup>2-4</sup> Numerous studies have shown links between industrialisation, environmental changes and pollution as possible causes.<sup>9-10</sup> This is a significant problem as the disease

Table 1: Patients' demographics and prevalence of symptoms of allergic rhinitis.

		Mean (SD)	Number of patients (%)
<b>Age (years)</b>		33.5 (15.5)	
<b>Gender</b>	<b>Male</b>		26 (26.5)
	<b>Female</b>		72 (73.5)
<b>Positive family history</b>			30 (30.6)
<b>Asthma</b>			24 (24.5)
<b>Eczema/skin rashes</b>			34 (34.7)
<b>History of sinus disease</b>			31 (31.6)
<b>Food allergy</b>			32 (32.7)
<b>Drug allergy</b>			11 (11.2)
<b>Symptoms</b>	<b>Nasal congestions</b>		86 (87.7)
	<b>Rhinorrhea</b>		72 (73.5)
	<b>Nasal Itch</b>		72 (73.5)
	<b>Sneezing</b>		70 (71.4)
	<b>Itchy eyes</b>		55 (56.1)
	<b>Itchy throat</b>		47 (48)
	<b>Post-Nasal drip</b>		46 (46.9)
	<b>Facial Pain</b>		42 (42.9)
	<b>Chronic Headache</b>		38 (38.8)
	<b>Chronic cough</b>		15 (15.3)

Table 2: SPT results and allergens reactivity frequency.

		Number of patients (%)
<b>SPT RESULTS (N=98)</b>	<b>Positive</b>	85 (86.7)
	<b>Negative</b>	13 (13.3)
<b>COMMON ALLERGENS TESTED IN POSITIVE SPT (N=78)</b>		
<b>Animal/Insect Allergens</b>	<b>House dust mite</b>	59 (69.4)
	<b>Blomia tropicalis</b>	52 (61.2)
	<b>Feline dander</b>	19 (22.4)
	<b>German cockroach</b>	18 (21.2)
<b>Food Allergens</b>	<b>Shrimp</b>	31 (36.5)
	<b>Wheat flour</b>	15 (17.6)
	<b>Chicken</b>	12 (14.1)
	<b>Fish</b>	11 (12.9)
	<b>Banana</b>	8 (9.4)
	<b>Milk</b>	7 (8.2)
	<b>Egg</b>	5 (5.9)
	<b>Peanuts</b>	4 (4.7)
<b>Aeroallergens</b>	<b>Bermuda grass</b>	8 (9.4)
	<b>Pollen</b>	5 (5.9)
<b>Monoallergens</b>		17 (20.0)
<b>2 to 6 allergens</b>		65 (76.5)
<b>≥11 allergens</b>		3 (3.5)



burden of AR is high, both in terms of the negative impact on a person's quality of life as well as significant total economic burden related to the disease.<sup>11</sup> The total economic burden of AR from all causes in the United States has been estimated to be around \$24.8 billion annually.<sup>12</sup> With the rapid development of Brunei and combined with worldwide environmental changes, the incidence of AR is expected to rise, hence an effective management strategy is needed in order to decrease the disease as well as economic burden.<sup>3,4</sup>

This study is the first to evaluate the prevalence of SPT positive AR as well as identifying the common symptoms and allergens associated with it in patients suspected of AR in Brunei. Nasal congestions represent the most common symptom experienced by 87.7% of patients in this study, followed by rhinorrhoea (73.5%), nasal itch (73.5%) and sneezing (71.4%). These and other symptoms such as itchy throat, postnasal drip, facial pain, chronic headaches and cough can cause significant negative impact on patients' quality of life in terms of loss of sleep, poor concentration, leading to reduce productivity, efficiency and physical nasal trauma from repetitive blowing and wiping of nose with tissues. These in turn cause stress as well as anxiety in the patient's professional and social life. The loss of productivity and efficiency contributes negatively to economic growth from days loss from work.

Diagnosis of AR is dependent on a combination of a positive clinical history and examination, a full blood count and nasal cytology showing eosinophilia and supported by a positive SPT to common allergens to which the patients are exposed to. Among patients presenting with clinical history, symptoms and signs suggestive of AR, SPT is only positive in 86.7% of our study population. Hence, based on clinical history and examination alone, 13.3% of patients were wrongly diag-

nosed as AR. These 13 patients showed a negative SPT to all 14 common allergens found in our region and their preliminary diagnosis were later amended to non-AR. It is important to distinguish between AR from non-AR as they have overlapping spectrum of symptoms but different treatment strategies.<sup>2,13</sup> SPT is an in-vivo test and determines the IgE antibodies present in the patient's skin to specific allergens. SPT is fast, cheap and a reliable method with low risk for anaphylaxis. A more expensive alternative in-vitro test is the radio-allergosorbant test (RAST), which quantifies the amount of allergen specific IgE antibodies in the patients' blood. Thus implementing SPT as a routine test for clinically suspected cases of AR can help to reduce cost of treating AR in appropriately since treatment for non-AR is different.

According to our study, indoor or animal and insect allergens accounts for majority of the cases of perennial AR in Brunei. Common allergens such as house dust mite and *Blomia tropicalis* which are present throughout the year, were positive in 69.4% and 61.2% of SPTs tested in our patients respectively. These results were similar to those found in other ASEAN countries such as Singapore and Malaysia where house dust mite and *Blomia tropicalis* accounts for over 70-80% of AR.<sup>6</sup> Feline dander allergens were only positive in 22.4% of SPTs which is lower than expected for a country where cats are popularly kept as house pets.

As expected, food allergens are generally not a major cause of AR in adults and like other studies, food allergens SPT were positive in less than 15% of the patients tested except for shrimp which showed the highest positive reaction at 39.7%.<sup>14,15</sup> Seasonal allergens such as Bermuda grass and pollen caused allergic rhinitis in 8% and 3% of studied subjects respectively, suggesting that seasonal allergic rhinitis is less common in Brunei Darussalam.

Gendeh *et al.* reported that majority of patients diagnosed with AR were allergic to more than one allergen, which was also consistent with our study findings.<sup>16</sup> Only 17 out of 98 patients were sensitive to mono-allergen. This can help explain why patients still experienced symptoms despite avoidance of the offending allergen and why testing multiple allergens via SPT are generally recommended.

Bronchial asthma can also co-exist with AR and in our patients, asthma was previously diagnosed in 24.5% of cases. Gendeh *et al.* reported higher percentage of co-existing bronchial asthma, which was present in 40-50% of patients with AR.<sup>15</sup> Nasal symptoms were reported in 75% of patients with bronchial asthma, which may mask the presence of AR.<sup>1</sup> With such intermixed and cross-over of symptoms, accurate diagnosis and treatment of AR is important. Thus, it is advisable for patients to be referred to ORL outpatient clinics for ENT consultation and SPTs.

The primary treatment for any allergic disease (including AR) is prevention by avoidance and so identifying the offending allergens is important. This study has identified the three most common allergens are the house dust mite, *blomia tropicalis* and shrimp. Patients and their families with a known history of allergy or atopy should be educated and warned to avoid these allergens as a primary preventive measure. To reduce exposure to house dust mites, patients and their families should be taught measures such as providing adequate ventilation in their house and workplace to decrease humidity to less than 50, regularly wash bedding at 60° C, encase pillow, mattresses and quilts in allergen impermeable covers and use vacuum cleaner with HEPA filter. They should also be informed to dispose of feather bedding, remove carpets and curtains, pets and stuffed toys from bedroom. Avoidance of *blomia tropicalis* by storing food such as

grains and lentiles in closed containers.

Secondary management with pharmacotherapy is aimed for symptoms control and the type of drugs used is dependent on the predominant symptoms. The most commonly reported symptoms in this study are nasal congestions, rhinorrhoea, nasal itch and sneezing which are best treated with anti-histamine (orally or intranasal) or intranasal corticosteroids.<sup>7</sup> Tertiary management with immunotherapy is generally recommended for those with monoallergen AR, which should be our future goal.<sup>7</sup>

### **Limitation**

This study was conducted at the ORL outpatient clinic at RIPAS Hospital which is a tertiary referral centre for the whole country and may have inherently introduced referral bias. Thus, the results may not be applicable outside of hospital settings. There are more than 200 allergens available in the market for testing. It is not possible to use all these for routine testing. We have elected to use the most common 14 allergens found in our region. Hence patients allergic to other allergens not included in this study will not provide a positive SPT and this is one of the limitations of this study.

### **CONCLUSION**

Our study represents the first study to evaluate the pattern of SPT of 14 common allergens in patients diagnosed clinically with AR in Brunei. Our data showed that household animal/insect allergens such as the house dust mite, *blomia tropicalis* and food allergens such as shrimp are the 3 commonest allergens with positive SPTs ranging from 30-80%. Our results can be used to guide treatment of patients with AR, in particular with education strategy advising patients to avoid these allergens through regular washing of household beddings and avoiding frequent consumption of shrimps.

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