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Sensitisation profile of Chinese allergic rhinitis patients and effectiveness of a joint allergy-ENT clinic

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Summary

Purpose House dust mite (HDM) is the predominant cause of allergic rhinitis (AR) in Hong Kong but remains under-diagnosed and -treated. The association between patient-reported outcome measures (PROMs) and nasoendoscopy findings for AR have also not been investigated. This study investigated the demographics, sensitisation patterns, quality of life, use of sublingual immunotherapy and the association of PROMs and nasoendoscopy findings in AR patients through the first allergist–otorhinolaryngologists AR joint (ARJ) clinic in Hong Kong.

K. S. H. Hui, T. S. Li and W. L. W. Lo contributed equally to the manuscript.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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Methods This single-centred, retrospective observational study was conducted between January 2021 and December 2021. Clinical data from AR patients attending the ARJ clinic were analysed to identify the prevalence of HDM allergens, change in PROMs and the association of PROMs with nasoendoscopy scores. **Results** The three most common sensitising HDM allergens were *Dermatophagoides pterynosinus* (94.4%), *Dermatophagoides farinae* (88.9%) and *Euroglyphus maynei* (88.9%). At the 13- to 32-week follow-up (median 28 weeks), patients who attended the ARJ clinic had significant improvement in Total Nasal Symptom Score (TNSS; $p=0.038$). The visual analogue scale (VAS) was associated with nasoendoscopy score ($p=0.018$). Patients using SLIT (sublingual immunotherapy) showed overall improvements in PROMs.

Conclusion The ARJ clinic significantly improved AR symptoms. SLIT was effective and safe for patients who failed conventional treatments. VAS positively correlated with nasoendoscopy findings. Testing for *Dermatophagoides pterynosinus* as a single agent during skin testing was sufficient for the diagnosis of HDM AR and should be prioritized when resources are restricted. Further studies should be done to investigate the treatment outcome of AR patients and the effectiveness of SLIT in the Chinese population.

Keywords House dust mite · Pyroglyphidae · Endoscopy · Sublingual immunotherapy · Hong Kong

Abbreviations

AR	Allergic rhinitis
ARIA	Allergic rhinitis and its impact on asthma
ARJ	AR joint
BT	<i>Blomia tropicalis</i>
DF	<i>Dermatophagoides farinae</i>
DP	<i>Dermatophagoides pteronyssinus</i>

ENT	Ear, nose and throat
GINA	Global Initiative for Asthma
HDM	House dust mite
HSD	Honestly significant difference
PROM	Patient-reported outcome measure
RQLQ	Rhinoconjunctivitis quality of life questionnaire
SCIT	Subcutaneous immunotherapy
SD	Standard deviation
SLIT	Sublingual immunotherapy
SPT	Skin prick test
TNSS	Total nasal symptom score
VAS	Visual analogue scale

Introduction

Being the only public hospital in Hong Kong to offer specialist immunology and allergy services, Queen Mary Hospital established the territory's first joint allergy and ear, nose and throat (ENT) AR clinic in 2020. The clinic received referrals from across the entire territory and selectively focused on the evaluation of patients with symptoms suggestive of moderate–severe allergic rhinitis, who were considered to possibly benefit from a comprehensive joint evaluation with specialists in immunology and allergy and otorhinolaryngology. This unique clinic allowed patients to be jointly assessed by allergists and otorhinolaryngologists during the same consultation sessions, with the availability of specialist-led interventions such as nasoendoscopy, allergy skin prick tests (SPT) and sublingual immunotherapy (SLIT).

Allergic rhinitis (AR) is an immunoglobulin E-mediated hypersensitivity reaction upon exposure to specific aeroallergens. It triggers inflammation of the nasal mucosa, which clinically presents as nasal congestion, nasal discharge, sneezing and nasal itchiness [1]. AR is prevalent, affecting around 10–20% of the global population [2]. Epidemiological studies estimated an AR prevalence of approximately 8–23% in ethnically comparable Chinese populations and 10–40% in Hong Kong [3–9]. The sensitization patterns of offending aeroallergens vary considerably across different populations [10]. Among AR patients in Hong Kong, the most common sensitized aeroallergens were reported to be house dust mites (HDM) (including *Dermatophagoides farinae* [DF], *Dermatophagoides pteronyssinus* [DP] and *Blomia tropicalis* [BT]), cockroach and cat dander [9]. However, the most recent update was more than 15 years ago and reports on cross-reactivity between aeroallergens remain scarce.

According to the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline, AR is classified based on symptom persistence and severity. Symptoms are considered 'persistent' if present more than 4 days a week, or otherwise as 'intermittent'. Severity is regarded as 'mild' if none of the following items are present: (1) sleep disturbance, (2) impairment of

daily activities, leisure and/or sport, (3) impairment of school or work and (4) troublesome symptoms; AR is regarded as "moderate–severe" if one or more of these items are present [11]. Despite these clear clinical definitions and known detrimental consequences, the burden of AR among Hong Kong Chinese has been seldom reported [12].

Nasoendoscopy serves as a useful adjunct in the diagnosis, assessment and screening for possible differential diagnoses of AR. There have been several studies evaluating the association of nasoendoscopy findings with AR symptoms but with inconsistent results, suggesting that nasoendoscopy may not be a reliable diagnosis of AR [13–15]. The association between patient-reported outcome measures (PROMs) and the nasoendoscopy findings was not investigated as well.

Currently, the general first-line management approach to AR includes allergen avoidance measures and conventional pharmacological treatments. The most common physical allergen avoidance measure is impermeable encasings of bedding. Three randomised controlled trials have found that such measure significantly reduce HDM concentration [16–18]. However, two of these studies found that there were no clinical benefits of impermeable beddings as an isolated intervention [17, 18]. Another common chemical allergen avoidance measure is using acaricides. Similarly, acaricides were found to significantly reduce HDM concentration both as a single measure, or in combination with other measures [19, 20]. Current conventional pharmacological treatments for AR include antihistamines, intranasal corticosteroids and leukotriene receptor antagonists [13].

If these therapies fail to achieve satisfactory symptom control in patients, immunotherapy can be considered. Immunotherapy aims to induce sustained tolerance to specific allergens via repeated administration of unmodified allergen extracts over 2 to 5 years [1, 21, 22]. There are two routes of administration, including subcutaneous immunotherapy (SCIT) and SLIT. SLIT is a safer choice of use than SCIT, and HDM SLIT has even been incorporated into the most recent Global Initiative for Asthma (GINA) guidelines [23]. Nonetheless, specific allergy avoidance advice and immunotherapy can only be offered if the underlying causative allergen(s) can be identified. The severe lack of specialists in immunology and allergy in Hong Kong also hinders access to immunotherapy or specialist evaluation [24]. The effectiveness of SLIT in Hong Kong AR patients has only ever been explored in one previous study [25].

Given the gaps in research among AR patients in Hong Kong, this study aimed to investigate the demographics, quality of life, sensitisation pattern and use of SLIT in AR patients in Hong Kong. The secondary outcome is to elucidate the association between PROMs and nasoendoscopy findings. The effectiveness of the territory's first and only allergy-ENT

joint clinic in the management of AR was also evaluated in this study.

Methods

Study participants

A retrospective cohort study was conducted among patients presented with suggestive findings of AR at the Immunology and Allergy and ENT ARJ Clinic at the Queen Mary Hospital in Hong Kong from January 2021 to December 2021. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. All patients with suggestive findings of AR and were referred to ARJ clinic were screened for eligibility. Patients seen at the ARJ clinic would be seen by both an allergist and otorhinolaryngologists, with nasoendoscopy and SPT to common aeroallergens performed. Among them, those who did not fulfil the ARIA diagnostic criteria, had negative SPT results or were diagnosed with alternative diagnoses by allergists/otorhinolaryngologists were excluded.

Demographics and clinical assessment

A combined questionnaire collecting patients' demographics and relevant clinical history was administered at each patient's first presentation to the ARJ clinic. The questionnaire encompassed AR duration, smoking status, medical comorbidities including a history of allergic conjunctivitis, asthma, atopic dermatitis, food allergy, drug history for treatment of any allergic diseases (use of antihistamines, intranasal corticosteroids, montelukast), as well as the Total Nasal Symptom Score (TNSS), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), visual analogue scale (VAS) for AR. TNSS was used to characterise the course of persistent rhinitis during the first and subsequent clinic visits [26]. In this study, it consisted of 5 components that assess patients' rhinitis symptoms (rhinorrhoea, nasal congestion, nasal itching, sneezing, difficulty sleeping due to nasal symptoms) based on the previous 12 h and 2 weeks. The time frame of each component was assessed with a severity score range between 0 to 3 (0 = nil, 1 = mild, 2 = moderate, 3 = severe). A mean score for each component was calculated and were combined to produce the total nasal symptom score with a maximum score of 15. RQLQ was a rhinitis-specific quality of life questionnaire, with 28 questions in 7 domains (activity limitation, sleep problems, nasal symptoms, eye symptoms, practical function and emotional function). Each question had a scale from 0 to 6 (0 = not impaired at all; 6 = severely impaired) [27, 28]. The maximum RQLQ score was 168. VAS evaluates the self-perceived severity of AR in patients. It consisted of a 10 cm line with 10 intervals (0 = completely under control; 10 = completely uncontrolled).

Nasoendoscopy was performed at each patient's first presentation to the ARJ clinic. A variation of categorical nasoendoscopy scoring system was adopted by otorhinolaryngologists for nasal and paranasal sinuses assessment [14]. The scoring system included 6 components (nasal polyps, turbinate hypertrophy, water discharge on nasal floor, mucopurulent discharge, mucosal oedema, pale mucosa). Each component was scored 0 or 1 (0 = no, 1 = yes). The maximum total score was 6.

Those with follow-up visits scheduled were assessed by the combined questionnaire comprising TNSS, RQLQ and VAS for AR in subsequent visits to evaluate the differences in symptom severity and quality of life after they were managed by the ARJ clinic compared to that at the first presentation to the clinic.

Immunological investigations

SPT was performed to confirm the diagnosis of AR at each patient's first presentation to the ARJ clinic. A variety of allergens were tested, including different species of house dust mites (*Acarus siro*, *BT*, *Chorotoglyphus arcuatus*, *DF*, *DP*, *Euroglyphus maynei*, *Glycyphagus domesticus*, *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*), German cockroach, Oriental cockroach, American cockroach, cat dander, dog dander, 7 grass mix (Timothy, Orchard, June, Redtop, Meadow Fescue, Perennial Rye, Sweet Vernal), 9 tree mix (Alder, White Ash, Black Birch, American Elm, Shagbark Hickory, Maple (Sugar), White Oak, White Poplar, American Sycamore), 4 weed mix (Cocklebur, Rough Pigweed, English Plantain, Lamb's Quarters) and mould mix (*Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*) (ALK, Hørsholm, Denmark). Histamine and normal saline were used as positive and negative controls respectively. Wheal size 3 mm larger than the wheal size of the negative control 15 min after the application of the allergen solution was considered a positive result [29].

Statistical analysis

Data were analysed by the Statistical Package for the Social Sciences (macOS version 27; SPSS Inc, Armonk, NY, USA). Venn diagrams were created using Jvonn [30]. Assumption of normality of continuous variables was tested using Shapiro–Wilk test. Values of categorical variables were reported as percentages, while values of continuous variables were reported as means ± standard deviation (SD) or medians with interquartile range if non-parametric. Scores obtained in TNSS, RQLQ and VAS were categorised into tertiles respectively for the analysis of the association of variance with nasoendoscopy scores. Paired t-test was conducted to compare the means of the three scores before and after the clinic visit. Descriptive analysis of the means of the three scores was done. One-way

analysis of variance (ANOVA) with Tuckey Honestly Significant Difference (HSD) test was used to analyse the mean difference between the categorised scoring of TNSS, RQLQ, VAS and nasoendoscopy score. The 2-tailed statistical significance level was set at the 5% level.

Results

Throughout the study period, 27 unique patients were referred to ARJ clinic for suspected moderate–severe and poorly controlled AR. All patients underwent comprehensive evaluation by both allergists and otorhinolaryngologists. After joint review, supported by nasoendoscopy and SPT findings, 7 patients were excluded due to negative SPT, while the

remaining 2 patients had positive SPT but the symptoms did not meet the ARIA guideline for AR. A total of 18 patients were diagnosed as having AR and included in this study (Fig. 1). These patients were provided with traditional management regimen which included allergen avoidance measures, antihistamines/intranasal corticosteroid/leukotriene receptor antagonists based on the clinical assessment. Baseline demographic, clinical features and nasoendoscopy findings are shown in Table 1. The median nasoendoscopy score at first ARJ clinic visit was 2.5 (IQR 1.0–4.0).

Fig. 1 Study flow chart. ARJ allergic rhinitis joint, SLIT sublingual immunotherapy

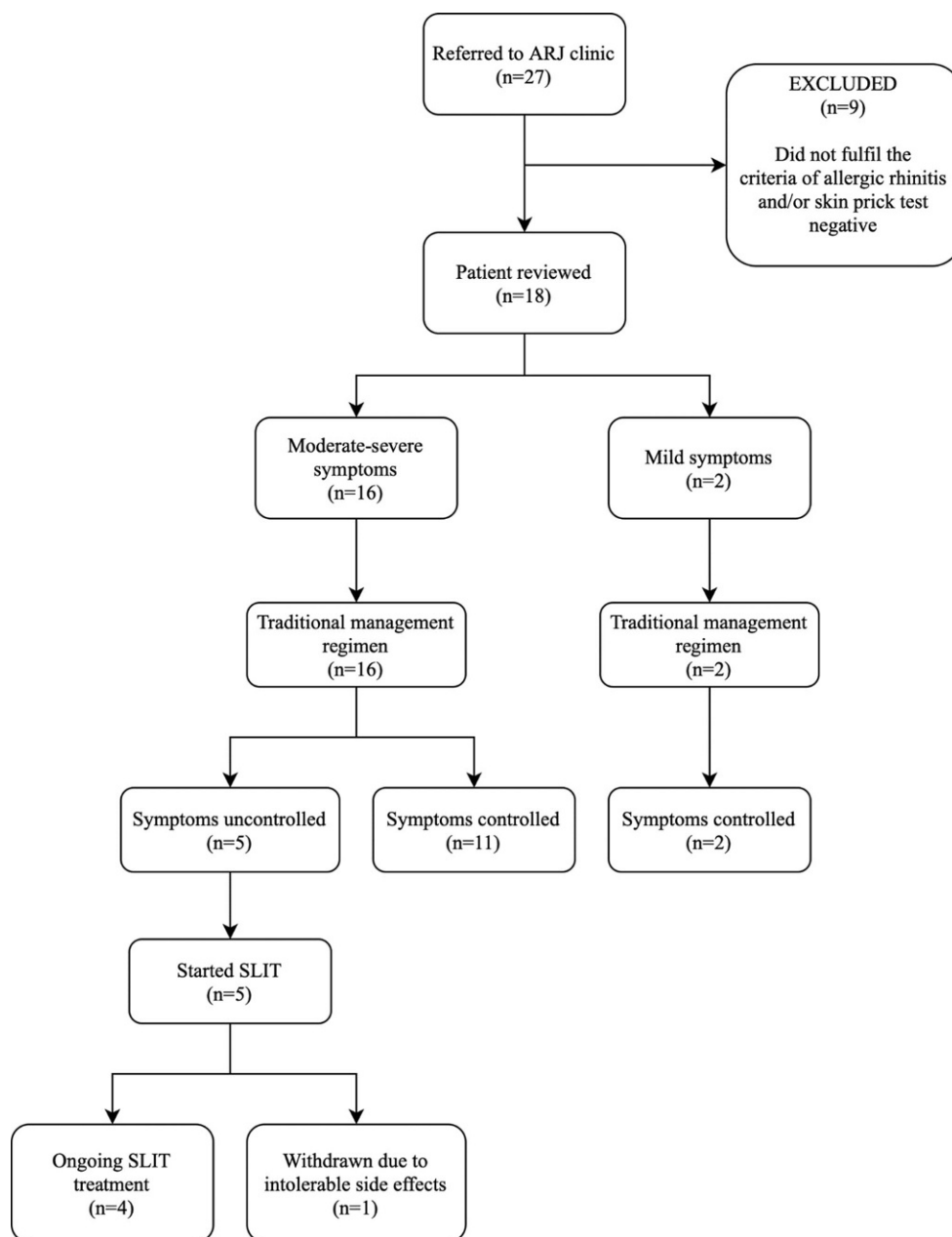


Table 1 Demographics and clinical features of AR patients at baseline. *N* = 18

Demographics	N (%)
Male sex	11 (61.1)
Age at first visit, years	33.8 ± 13.3
Smoking	2 (11.1)
Clinical features	N (%)
History of AR, years	11.5 (9.5–27.8)
Persistent symptoms	11 (61.1)
Moderate-severe symptoms	17 (94.4)
Anosmia	3 (16.7)
Allergic comorbidities	
Atopic dermatitis	9 (50.0)
Asthma	6 (33.3)
Allergic Conjunctivitis	4 (22.2)
Food Allergies	2 (11.1)
AR treatments prior to ARJ clinic	
Antihistamines	11 (61.1)
Intranasal corticosteroids	13 (72.2)
Leukotriene receptor antagonists	3 (16.7)
Patient-reported outcome measures	
Total Nasal Symptom Score	5.19 ± 1.62
Rhinoconjunctivitis QOL Questionnaire	28.8 ± 15.2
Visual analogue score	4.9 ± 1.7
Nasoendoscopy score	2.5 (1.0–4.0)
Nasoendoscopy findings	
Mucosal oedema	10 (55.6)
Turbinate hypertrophy	10 (55.6)
Watery discharge on nasal floor	9 (50.0)
Mucopurulent discharge	4 (22.2)
Nasal polyp	4 (22.2)
Pale mucosa	2 (11.1)

Continuous data were presented as mean ± standard deviation or median (25th to 75th percentile); categorical data were presented as percentages
QOL quality of life, AR(J) allergic rhinitis (joint)

DP, DF, EM were the three most common HDM allergens

The sensitisation profile of all patients was shown in Fig. 2. The most commonly sensitised allergens were DP (94.4%), DF (88.9%) and EM (88.9%); 17 (94.4%) patients were sensitised to at least one of these three house dust mite allergens. The remaining 1 (5.6%) patient was sensitised only to grass mix, while 15 (83.3%) patients were sensitised to all DP, DF and EM. Furthermore, 1 (5.6%) patient was sensitised to DP and DF but not EM, and 1 (5.6%) patient was sensitised to DP and EM but not DF (Supplementary Fig. 1).

Patients attending ARJ clinic had significant improvement in TNSS

Among the subgroup of patients whose questionnaire assessment results in the subsequent ARJ clinic visit were available (*N* = 13), there was a significant im-

provement in TNSS score between their baseline and follow-up visits (Fig. 3). The mean TNSS score at the first presentation to the ARJ clinic was 5.0 (SD 1.74). It decreased to 3.0 (SD 2.14) in the subsequent clinic visit ($t = -2.734$, $p = 0.018$). Changes in VAS ($t = -1.49$, $p = 0.161$) and RQLQ ($t = 0.920$, $p = 0.376$) did not reach statistical significance. The median duration between follow-ups was 28 weeks (range 13–32 weeks).

VAS was associated with nasoendoscopy score

Analysis of variance (Supplementary Table 1) showed that the nasoendoscopy score at the first presentation to the ARJ Clinic is associated with tertiles of VAS on the same occasion (*N* = 18). The mean nasoendoscopy score among those with tertile 3 VAS was 5.00 (SD 1.00), while that among those with tertile 1 and tertile 2 VAS were 2.1 (SD 1.73) and 2.14 (SD 1.57) respectively ($p = 0.038$). A post hoc Tukey HSD test (Supplementary Table 2) was conducted to elucidate inter-tertile relationship, which revealed statistically significant differences between the mean of nasoendoscopy score and VAS in 2 combinations: tertile 1 with tertile 3 ($p = 0.043$) and tertile 2 with tertile 3 ($p = 0.049$).

Improvements in PROMs were seen in patients starting SLIT

Patients who had initiated SLIT (*N* = 5) generally had a decreasing trend of TNSS, RQLQ and VAS after the start of treatment, indicating improvement in AR symptom severity and quality of life (Fig. 4). Overall, SLIT was well tolerated except for one patient who developed delayed hypersensitivity reactions around her lips after taking SLIT for 2 weeks. Symptoms were self-resolved with symptomatic medication and cessation of SLIT. The clinical details of patients prescribed SLIT were shown in Supplementary Table 3. The median duration between each follow-up for patients on SLIT is 13 weeks.

Discussion

Our ARJ clinic is the only dedicated AR clinic with joint allergist-otorhinolaryngologists expertise in Hong Kong. For patients with moderate-severe AR, the availability of specialist intervention such as nasoendoscopy, allergy testing and immunotherapy is essential to reduce misdiagnosis, optimise management and improve patient outcomes. Despite this, none of our patients had ever undergone an allergist or ENT evaluation prior to attending the ARJ clinic, highlighting the severe deficit in specialist care for AR patients in Hong Kong. In view of the positive outcomes and experience of our ARJ clinic, we propose such dedicated joint specialist clinics should be more widely adopted across the territory.

In this study, we demonstrate the effectiveness of the ARJ clinic on the improvement of AR symptoms.

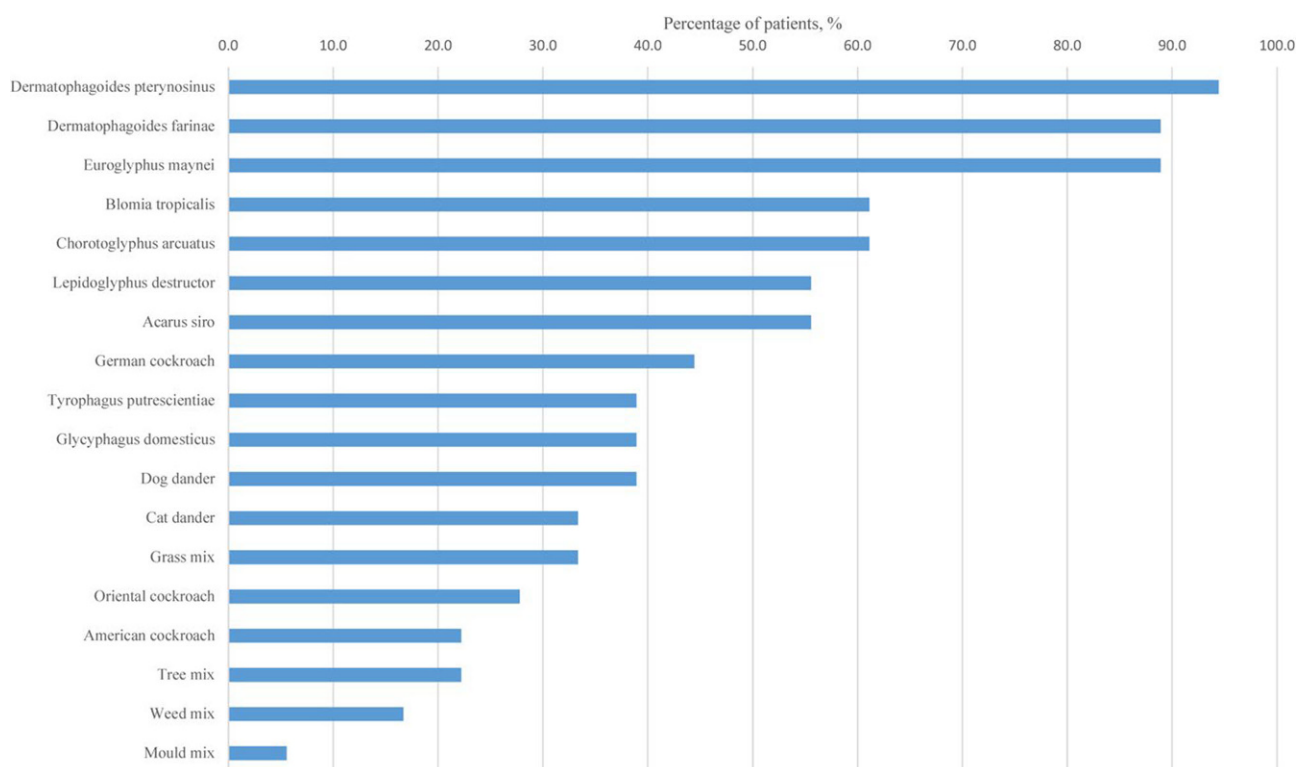


Fig. 2 Sensitisation profile of sensitised allergens in skin prick tests (SPT). *N* = 18

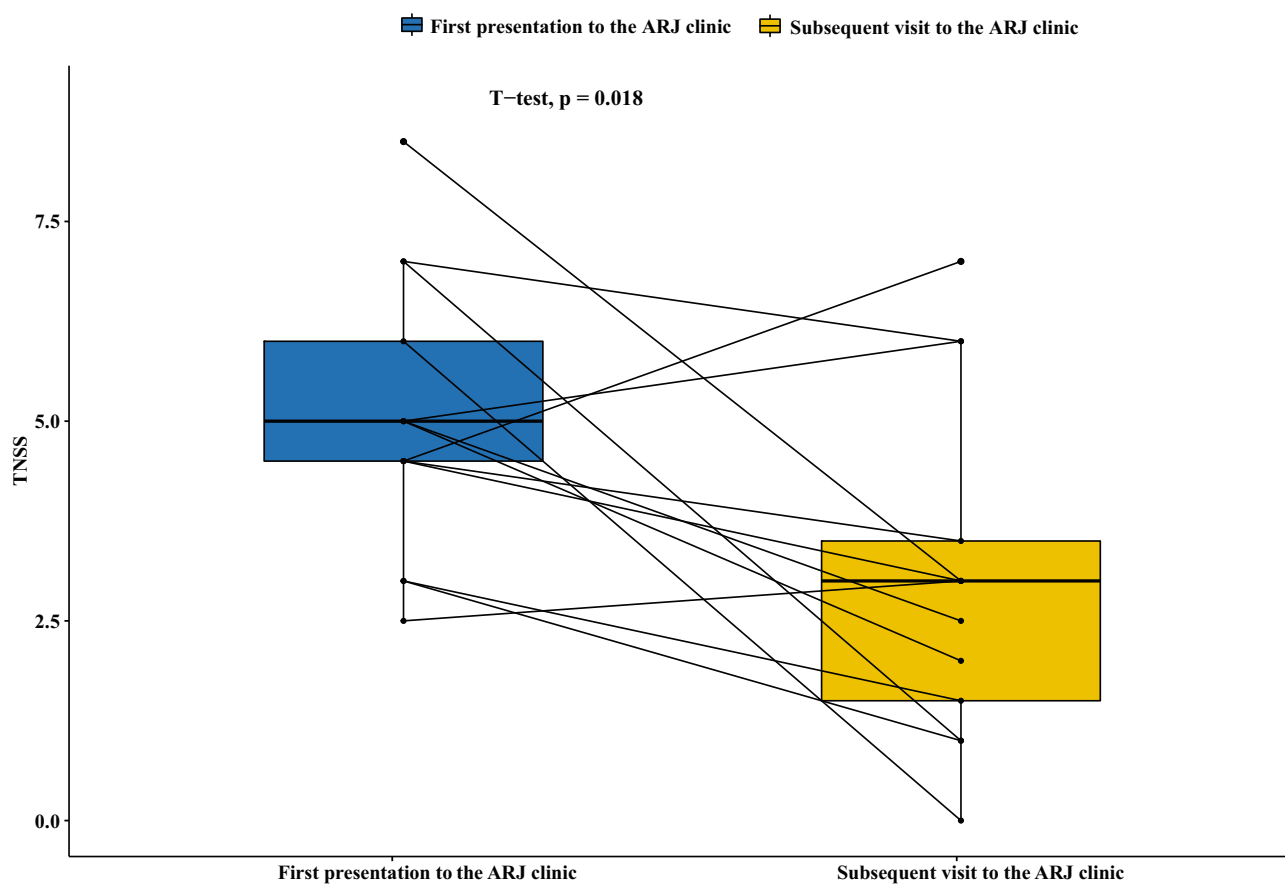


Fig. 3 Box plots of the paired t-test between baseline and follow-up Total Nasal Symptom Score (TNSS). *N* = 13

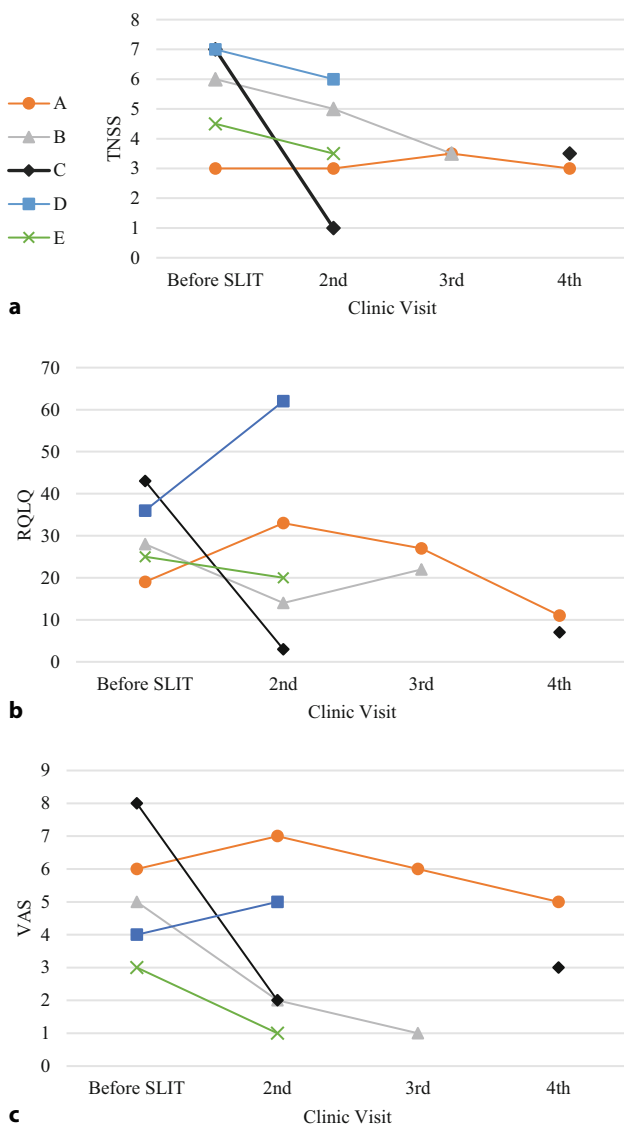


Fig. 4 Longitudinal Total Nasal Symptom Scores (TNSS), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores, visual analog scores (VAS) of sublingual immunotherapy (SLIT) patients. $N=5$; A–E indicate individual patients

Longitudinal mean TNSS score showed the most substantial improvement out of all PROMs. Although no significant difference was detected in longitudinal RQLQ and VAS, this may have been due to the limited sample size or reflects the insensitivity of these PROMs. For example, it is known that relatively small changes in AR symptoms (especially nasal obstruction and pruritus, as opposed to rhinorrhoea and sneezing) may not be reflected in the overall RQLQ score [28, 31].

We also identified that among all patients with moderate–severe AR, the most prevalent aeroallergens were the HDM species of *DP*, *DF* and *EM*. This is consistent with previous reports, especially as *DP* and *DF* are known to cohabit [32, 33]. Interestingly, all HDM AR patients were sensitised to *DP*, making the sensitivity of using *DP* to diagnose HDM AR 100%.

This has important implications, especially in Hong Kong. Firstly, we propose local centres consider prioritizing testing for *DP* for SPT to diagnose suspected HDM AR in our locality—especially when allergy facilities or expertise is limited. Secondly, such strong sensitization to *DP* may suggest a better response to HDM SLIT in our patients, as the sole registered formulation available in Hong Kong only targets *DP* and *DF* (Acarizax; ALK-Abello, Horsham, Denmark). Long-term prospective local studies will be required to evaluate this.

Nasoendoscopy is extremely useful for accurate diagnosis and evaluation of AR and more importantly to rule out other causes of nasal symptoms such as nasal polyposis, tumour, malignancy and nasopharyngeal carcinoma. Although readily available to otorhinolaryngologists, nasoendoscopy is not easily accessible in the primary care setting or medical units. Our study also identified a significant difference between the nasoendoscopy scores between high VAS scores and medium/low VAS scores. Therefore, we propose the VAS can be employed as a surrogate or predictor of the likeliness of positive nasoendoscopy findings. It may serve as a rapid and useful screening tool when prioritizing or selecting patients toward limited nasoendoscopy sessions. This would be especially useful in resource-limited settings, such as when specialist services may not be readily available or restricted during the COVID-19 pandemic.

Despite good compliance to traditional first-line AR medications, such as the combination of intranasal corticosteroids and antihistamines, over a quarter of patients still suffered from moderate–severe symptoms with substantial decrease in quality of life. HDM SLIT was offered for such patients with evidence of HDM sensitization with good response, with 80% demonstrating improvement in symptom control as reflected by the decreasing TNSS, RQLQ and VAS. Our experience is in line with other reports HDM SLIT efficacy [25, 34]. SLIT was also very safe and was tolerated very well in almost all patients. Only one patient experienced mild local adverse drug reaction, which rapidly resolved after cessation of therapy. This is consistent with the proven safety profile of SLIT with only 11 SLIT-associated anaphylaxis (all non-fatal) had been reported over more than 30 years since its introduction [22, 35]. Our experience corroborates this, and we demonstrate that SLIT is effective for our moderate–severe HDM AR patients in Hong Kong.

This study has several limitations. Since this was a pilot study, the small sample size limited our ability to analyse the effectiveness of SLIT in our cohort. Furthermore, patients' duration of SLIT administered was short compared to the standard guideline of about 3 years, so the reported effect on symptom control may be underappreciated [36]. In addition, there was an incomplete questionnaire for the third SLIT follow-up clinic visit of a patient. Considering the patient's completed questionnaire on the fourth visit,

a decreasing trend can still be observed. Due to the limited number of patients who were on SLIT, subgroup analysis was also not possible to investigate the SLIT effectiveness for AR patients presented with anosmia and experienced minimal improvement after nasal polypectomy. The inadequate size also potentially contributed to the poor consistency of RQLQ compared to other measurements. Similarly, the sensitisation pattern may not reflect the true distribution in Hong Kong population due to the small sample size. Since there are varying ways of practicing allergology in different countries, our findings and suggestions only reflected the situation in Hong Kong. This warrants future larger cohort investigations of the treatment outcome of AR patients with and without nasoendoscopy, and to evaluate the effectiveness and safety of SLIT in Chinese patients when the whole course of therapy is completed.

Conclusion

We demonstrate the effectiveness and utility of a dedicated AR clinic with joint allergist–otorhinolaryngologists expertise in Hong Kong. We identified the sensitization profiles of patients with moderate–severe AR and recommend that skin testing with *DP* alone may be sufficient in diagnosing HDM AR in our population. Furthermore, we propose that patient-reported VAS may be a useful predictor of allergic rhinitis symptoms or severity, especially when specialist facilities may not be so accessible. However, VAS should not replace nasoendoscopy for its diagnostic power to rule out other rhinopathologies. Lastly, we demonstrate the efficacy and safety of HDM SLIT among selected patients and highlight the need for dedicated and larger local studies in the future.

Author Contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by K. S. H. Hui, T. S. Li, W. Y. W. Lo, A. K. C. Kan, W. Y. W. Yeung, J. C. Y. Wong, S. Y. Ho, B. Y. H. Wong and P. H. Li. The first draft of the manuscript was written by K. S. H. Hui, T. S. Li, W. Y. W. Lo, A. K. C. Kan, W. Y. W. Yeung, P. H. Li and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

Conflict of interest K.S.H. Hui, T.S. Li, W.L.W. Lo, A. Kan, S. Ho, W. Yeung, J. Wong, V. Chiang, B.Y.H. Wong, and P.H. Li declare that they have no competing interests.

Ethical standards This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. Reference number: UW22-509. Informed consent was obtained from all individual participants included in the study.

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