

Self-Reported Allergic Rhinitis Prevalence and Related Factors in Civil Aviation Aircrew of China

Yin Bai; Mosheng Hu; Fengjie Ma; Ke Liu; Haijun Xu; Xuan Wu; Hongtian Wang

- INTRODUCTION:** Allergic rhinitis (AR) is a global health problem with gradually increasing prevalence. No large-scale, systematic, and comprehensive study on AR among civil aviation aircrew of China has been reported. We aimed to demonstrate the prevalence of and risk factors for self-reported AR among Chinese civil aviation aircrew.
- METHODS:** This study randomly surveyed 4059 civil aviation aircrew members from 12 cities in mainland China. A structured questionnaire was tailored, designed, and electronically delivered to all participants. Based on self-reported results, prevalence of and risk factors for AR were calculated/analyzed.
- RESULTS:** The prevalence of self-reported AR was 23.38%. Among aircrew members, 10.37% presented with ear barotraumas, whereas 9.95% reported symptom aggravation during flight. Of aircrew members, 10.32% had symptoms related to flight duration, whereas 4.43% of symptoms related to flight altitude. Significant differences between rhinorrhea and sneezing, as well as between nasal itching and sneezing, were observed in the Total Nasal Symptoms Scores (TNSS). The Rhino-conjunctivitis Quality of Life Questionnaire (RQLQ) showed significant correlation between each section. TNSS was significantly related to RQLQ. Both TNSS and RQLQ significantly correlated with flight time.
- CONCLUSIONS:** The prevalence of self-reported AR among civil aviation aircrew is higher than the general population in China. The severity of nasal symptoms and complications are significantly associated with quality of life and flying duties.
- KEYWORDS:** allergic rhinitis, self-reported prevalence, civil aviation, aircrew.

Bai Y, Hu M, Ma F, Liu K, Xu H, Wu X, Wang H. *Self-reported allergic rhinitis prevalence and related factors in civil aviation aircrew of China. *Aerospace Med Hum Perform.* 2021; 92(1):25–31.*

Allergic rhinitis (AR) is an inflammatory disease involving nasal mucosa and induced by immunoglobulin E (IgE) mediated reaction in allergen-sensitized subjects. It is characterized by clinical symptoms of rhinorrhea, sneezing, nasal congestion, and nasal itching. In 2013, the World Allergy Organization (WAO) published a white paper on allergies, pointing out that global allergic diseases have caused a huge burden to both developed and developing countries, among which AR is one of the most common types of allergic diseases.¹⁸

AR is a typical aeromedical problem with variable timing and severity of symptoms that relate to the occurrence of aerotitis media and aero-sinusitis that are frequently encountered during periodical medical certification. Complications of AR, such as asthma, allergic dermatitis, eczema, sinusitis, nasal polyps, and upper airway cough syndrome, exert adverse effects on quality of life and flying duties. Importantly, public safety is at significant risk when flying duties are undertaken with

uncontrolled AR or with the use of restricted antihistamines, which have sedating effects and negatively impact an individual's availability to conduct flying duties.²⁰

Although self-reported AR in civil aviation aircrew has been previously reported, only a small sample size of Chinese aircrew had been represented. Lack of representativeness could potentially limit evidence available to develop appropriate policies for effective certification. Based on an electronic questionnaire, we conducted a survey on self-reported AR and analyzed risk

From the Civil Aviation Medical Assessment Institute, Civil Aviation Medicine Center, Civil Aviation Administration of China (CAAC), Beijing, China.

This manuscript was received for review in July 2020. It was accepted for publication in October 2020.

Address correspondence to: Hongtian Wang, Department of Allergy, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China; wht301@263.net or Fengjie Ma, Civil Aviation Medical Assessment Institute, Civil Aviation Medicine Center, Civil Aviation Administration of China (CAAC), Beijing 100123, China; mafengjie@163.com.

Reprint & Copyright © by the Aerospace Medical Association, Alexandria, VA.

DOI: <https://doi.org/10.3357/AMHP:5727.2021>

factors in Chinese civil aviation aircrew members in 12 cities from March to April 2020.

METHODS

Subjects

The aircrew members of the Civil Aviation Administration of China (CAAC) include pilots, navigators, flight mechanics, flight correspondents, and flight attendants. The majority of them are pilots and flight attendants. There are nearly 70,000 Chinese civilian pilots, with a male-to-female ratio of 52:1 and 140,000 Chinese civilian flight attendants, with a male-to-female ratio of 1:9. In this study, a structured questionnaire was tailored and a random recruitment was conducted to investigate prevalence of self-reported AR in 4059 civil aviation aircrew members. Informed consent was provided by all participants prior to inclusion. This study was approved by Ethical Committee of our institution.

Questionnaire

The questionnaire consisted of two parts. The first part was a screening questionnaire used to gather information on seven questions regarding gender, age, occupation, resident city, total flight hours, flight hours in last year, and diagnosis of AR. Each participant was asked the following questions: ‘In the past 12 mo, have you ever had a problem with rhinorrhea, sneezing, nasal congestion, or nasal itching when you are exposed to allergens (after excluding upper respiratory infection or influenza)?’ If the answer was ‘yes’, the participant continued to specific questions in the second part, consisting of three sections to gather information on: 1) a history of AR, self-reported allergens (triggers), complications, a history of nasal surgery, family history of allergic diseases, duration and severity of nasal symptoms, perennial AR or seasonal AR, skin prick test and/or serum specific IgE test, whether ear barotraumas were related to AR during flight? Whether AR symptoms were aggravated during flight? Whether AR symptoms were related to flight duration and flight altitude? 2) The Total Nasal Symptoms Score (TNSS) scale included rhinorrhea, sneezing, nasal congestion, and nasal itching. A score of 0 to 4 indicated severity of symptoms, where: 0 was asymptomatic, 1 for mild, 2 for moderate, 3 for severe, and 4 for extremely severe. 3) The Rhino-conjunctivitis Quality of Life Questionnaire (RQLQ) scale included 28 terms in 7 sections. A score of 0 to 6 indicated the different extent of activities which were interfered with by nasal/eye symptoms, where: 0 = no trouble, 1 = almost no trouble, 2 = some trouble, 3 = medium trouble, 4 = quite troubled, 5 = very troubled, and 6 = extremely troubled.

AR was then diagnosed with criteria consistent with the allergic rhinitis and its impact on asthma (ARIA) guidelines.³ Severity and duration of AR were classified accordingly as mild, moderate/severe, intermittent, or persistent. According to course duration, AR was divided into perennial AR and seasonal AR. All participants completed a screening questionnaire.

Self-reported AR subjects continued to complete the second part while the nonallergic rhinitis subjects were automatically terminated.

Statistical Analysis

Statistical analysis was performed with SPSS version 23 (IBM, Armonk, NY, USA). The normality of distribution was assessed using the Kolmogorov-Smirnov test. The TNSS and RQLQ failed to conform to normal distribution, so nonparametric tests were conducted. The rank sum test of multiple independent samples and Spearman rank correlation analysis were used to analyze differences. *P*-values < 0.05 were considered statistically significant.

RESULTS

A total of 4059 civil aviation aircrew members were surveyed. Among them, 949 had self-reported AR, with a male-to-female ratio of 5:7, and mean age of 31.4 ± 9.6 (range: 18–59 yr). The overall prevalence of self-reported AR was 23.38%. Among 1076 pilots, 221 (20.54%) had self-reported AR. Among 2983 flight attendants, 728 (24.40%) had self-reported AR. A total of 336 aircrew members with AR had completed a skin prick test and/or serum specific IgE test, of whom 299 had positive allergens while 37 had negative ones. Of 949 patients with self-reported AR, 45 (4.74%) had a history of nasal surgery. The percentage of perennial AR or seasonal AR was 20.97% (199/949) or 79.03% (750/949), respectively. Persistent AR and intermittent AR accounted for 30.14% (286/949) and 69.86% (663/949), respectively. All patients were classified as mild [56.69% (538/949)] and moderate/severe [43.31% (411/949)], respectively. The distribution of self-reported AR in different cities is listed in **Table I**. The highest and lowest prevalence of self-reported AR was 38.40% in Shijiazhuang and 10.53% in Zhengzhou, respectively.

Among 949 aircrew members with self-reported AR, 322 cases had been working for more than 10 yr. There were 264 cases who had a total flight time $\geq 10,000$ h and 430 had a flight time ≥ 900 h in the last year. A total of 10.37% of aircrew members had ear barotraumas and 9.95% suffered from symptoms aggravation during flight. Also, 10.32% of aircrew members

Table I. Geographic Distribution of Self-Reported Allergic Rhinitis (AR).

CITY	COMPLETED SCREENING QUESTIONNAIRE		PREVALENCE OF AR (%)
	QUESTIONNAIRE	SELF-REPORTED AR	
Shenyang	1045	281	26.89
Chongqing	807	186	23.05
Beijing	371	111	29.92
Kunming	598	101	16.89
Jinan	302	57	18.87
Shijiazhuang	125	48	38.40
Chengdu	172	39	22.67
Guangzhou	112	22	19.64
Nanjing	129	30	23.26
Xian	156	42	26.92
Shanghai	109	18	16.51
Zhengzhou	133	14	10.53

cases

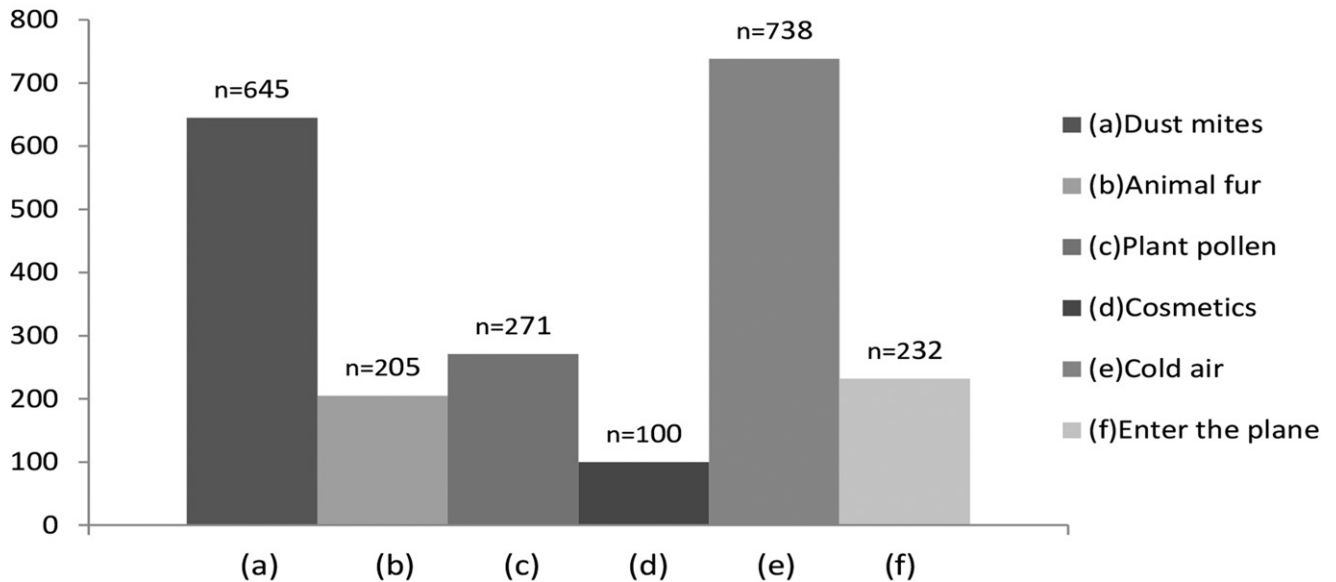


Fig. 1. Type and number of self-reported allergens (triggers) in this study.

had symptoms related to flight duration whereas 4.43% related to flight altitude.

Self-reported allergens (triggers) causing AR under certain circumstances are listed in **Fig. 1**. The top three self-reported allergens were cold air, dust mites, and plant pollen. Of AR patients, 17.7% had a family history of allergic diseases. Positive association between AR and family history of allergic diseases are described in **Fig. 2**. Complications of AR, such as nasal polyps, sinusitis, asthma, allergic dermatitis, and eczema, occurred either separately or concomitantly. In our study, the most common allergic diseases associated with AR in aircrew members were allergic dermatitis, sinusitis, and eczema (**Fig. 3**).

The TNSS scores for rhinorrhea, sneezing, nasal congestion, and nasal itching were similar at 1.00 (range: 1.00~2.00). As shown in **Table II**, four nasal symptoms of the TNSS scale were related to AR ($\chi^2 = 16.142, P < 0.05$). Based on multiple comparisons, significant differences between rhinorrhea and sneezing, as well as between nasal itching and sneezing, were observed (correction $P \approx 0.0083$).

The RQLQ scores from section 1 to 7 were 3.00 (2.00~6.00), 3.00 (0.00~6.00), 7.00 (0.00~12.00), 4.00 (2.00~6.00), 6.00 (3.00~8.00), 4.00 (0.00~7.00), and 4.00 (0.00~6.00), respectively. Furthermore, correlation analysis (r_p ranged from 0.626 to 0.919) is listed in **Table III**. Notably, practical problems (wipe

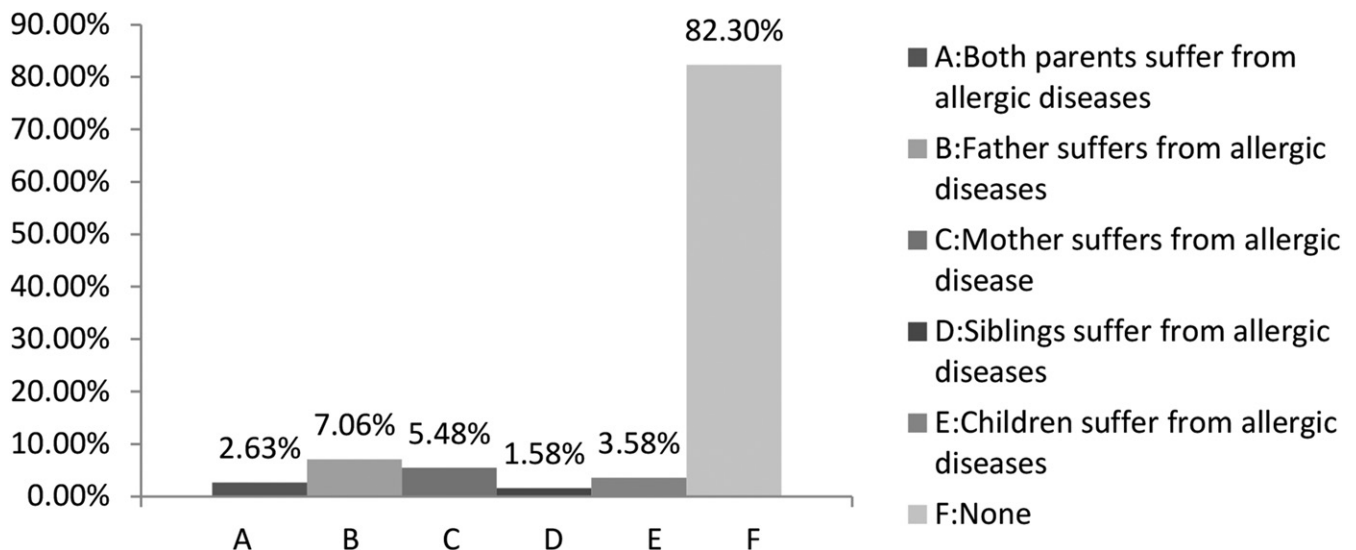


Fig. 2. Percentage of members with a family history of allergic diseases.

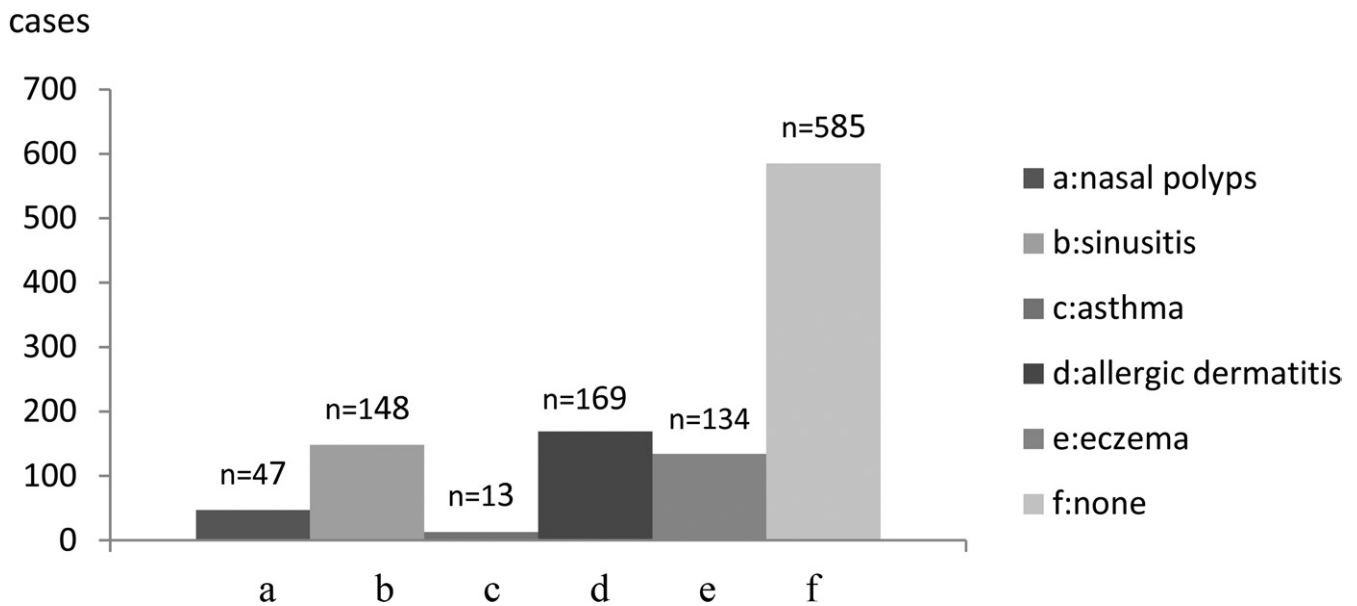


Fig. 3. Number of self-reported allergic rhinitis cases with comorbidities (other allergic diseases).

nose/eyes and blow nose repeatedly), activities (flight work, indoor activities, outdoor sports) and performances (less enthusiasm for life, thirst, reduced ability to work, tired, inattention, headachy, exhausted) were closely related to AR symptoms.

The total score of the TNSS scale was significantly correlated with the RQLQ scale ($P < 0.001$; $r_p = 0.694$). As shown in **Table IV**, total scores of the TNSS and RQLQ scales were significantly correlated with total flight time and flight time in the last year ($P < 0.001$), respectively.

DISCUSSION

Currently, global prevalence of AR is up to 10–40%, which has a serious impact on patients' quality of life.² AR is the fifth most common chronic disease in the United States. It is estimated to affect nearly 1 in every 6 Americans and generates large health expenditures annually.²² In addition, prevalence of AR in Germany is as high as 24%, increasing year by year.²³ Japanese guidelines for AR in 2017 indicated prevalence of AR in Japan being increased from 29.8% in 1998 to 39.4% in 2008.¹⁷ At present, the prevalence of AR among civil aircrew members in China is rarely reported. Zhang et al. conducted a multicenter survey in 2004–2005 and calculated prevalence of self-reported

AR in Chinese adults from 11 cities to be 11.1%.²⁹ Furthermore, they conducted another AR survey in 18 cities of China and reported a prevalence of 17.6% in 2011.²⁷ In a short period of 6 yr, the number of AR patients in China had been increased by nearly 100 million. This has aroused particular concern about the prevalence of AR in Chinese civil aviation aircrew members.

Mainland China contains seven geographic areas: Northeast, North, Northwest, Middle, East, South, and Southwest.²⁷ This survey from 12 cities covered all seven geographic areas, which displayed considerable differences regarding topography, climate, air pollution, allergens, and socioeconomic status. All these factors might have separate or combined influences on participants' lifestyle and prevalence of self-reported AR.

In this study, the prevalence of self-reported AR in aircrew members (23.38%) is higher than the general population (17.6%) in China. One reason may be our survey was conducted in the pollen period (March~May) and it is the latest data. The other reason may be the environment and conditions between the two groups were largely different. The fifth section of the RQLQ scale (nasal symptoms) had a good consistency with the TNSS score. The average age of subjects in this survey was 31.4 ± 9.6 yr, indicating that the age composition of aircrew members is getting younger in China.

Previous studies proposed that prevalence and severity of AR were closely correlated with different levels of pollen allergens in the natural environment.^{1,11} As shown in Fig. 1, the top three sensitizers in this study were cold air, dust mites, and plant pollen. In combination with the daily working environment and living conditions of aircrew the following conditions may apply. 1) Aircrew members often cross different regions and time zones, and thus experience seasonal alternations, day and night shift, and temperature changes. In addition, cold air is easy to stimulate nasal hyperreactivity. 2) Aircrew members often have to spend the night

Table II. Differences in Symptoms from the Total Nasal Symptoms Score (TNSS).

SYMPTOM GROUP	MEAN RANK	χ^2	P
A-B	966.18-932.82	2.076	0.150
A-C	967.85-931.15	2.479	0.115
A-D	927.17-971.83	3.733	0.053
B-C	951.63-947.37	0.033	0.855
B-D	909.96-989.04	11.777	0.001
C-D	908.82-990.18	12.297	<0.001

A: nasal congestion, B: rhinorrhea, C: nasal itching, D: sneezing. P-value < 0.0083 was considered statistically significant.

Table III. Correlation Analysis Among Seven Sections of the Rhino-conjunctivitis Quality of Life Questionnaire (RQLQ) Scale ($N = 949$).

SECTIONS	r_p	P	SECTIONS	r_p	P	SECTIONS	r_p	P
1-2	0.733**	<0.001	2-4	0.668**	<0.001	3-7	0.832**	<0.001
1-3	0.788**	<0.001	2-5	0.708**	<0.001	4-5	0.885**	<0.001
1-4	0.789**	<0.001	2-6	0.719**	<0.001	4-6	0.746**	<0.001
1-5	0.814**	<0.001	2-7	0.745**	<0.001	4-7	0.750**	<0.001
1-6	0.714**	<0.001	3-4	0.745**	<0.001	5-6	0.745**	<0.001
1-7	0.740**	<0.001	3-5	0.782**	<0.001	5-7	0.750**	<0.001
2-3	0.829**	<0.001	3-6	0.766**	<0.001	6-7	0.797**	<0.001

1: activity, 2: sleep, 3: performance, 4: practical problems, 5: nasal symptoms, 6: eye symptoms, 7: emotions; r_p : Spearman correlation coefficient.

** $P < 0.01$, indicating significantly correlated.

abroad and accommodation hotels are usually carpeted. Bedding and sofa cushions can carry parasitic dust mites. 3) Carpets, blankets, and seats in airplane cabins are ideal places where dust mites live. Furthermore, air purification and circulating filtration equipment cannot completely remove dust mites. 4) Some patients decorate their bedroom with a carpet that creates an environment for dust mites. 5) Seasonal AR is easily affected by plant pollen in spring and autumn. Even if aircrew members are temporarily away from a suspended layer of pollen during flight, it is difficult to avoid allergens completely in daily life.

AR is attributed to a combination of genetic, epigenetic, and environmental factors.^{4,9,15} As early as in 1997, Noguchi et al. proposed when both parents had AR, prevalence of AR in their children could be as high as 75%. If one parent had AR, prevalence of AR among their children could be as high as 50%, which underscores the important role of family history.¹⁶ A systematic review of siblings and twins indicated that genetic factors play a greater role than early-life environmental factors in the atopic march.¹³ In our study, 17.7% of aircrew members had a family history of allergic diseases, mainly manifested in their fathers, mothers, or children suffering from allergic diseases. In addition, prevalence of AR in siblings reached 1.58% in our study, indicating an important role of genetic factors in the pathogenesis of AR (Fig. 2).

As an upper airway disease, AR is related to development of other allergic diseases. Previous studies suggest that AR closely correlates with allergic dermatitis, eczema, apnea, sinusitis, nasal polyps, and upper airway cough syndrome. Nasal congestion caused by AR has a prominent role in sleep impairment, so that treatments for AR can improve patients' sleep disorders.^{3,5,30} For aircrew members, more attention should be paid to the internal connection between AR and allergic diseases. House dust mites are the main allergen causing AR and are an important risk factor for allergic respiratory diseases.¹² A nasal stimulation test can increase eosinophil inflammation in the upper and lower airways

of children who are allergic to mites. In addition, the nasal stimulation test can not only cause and accelerate airway inflammation, but also lead to high reactivity in the upper and lower airways in patients with persistent AR without asthma symptoms.²⁶ Allergic dermatitis, sinusitis, and eczema are the main allergic diseases associated with AR in our study (Fig. 3). During a 5-yr follow-up of children with atopic dermatitis, 36 patients also had asthma, 33 had AR, and 13 had both diseases.⁶ Therefore, aircrew members with AR and allergic dermatitis should be paid more attention to prevent asthma. In our study, 13 flight attendants with AR developed asthma, which may be life-threatening if rescue is not timely during flight.

In recent years, many studies on airway models for upper and lower airway inflammation have confirmed that upper and lower airways share common physiological and pathological mechanisms, and similarity of their structures constitutes the basis of consistency in inflammation. AR is an important risk factor for asthma and impairs clinical management of asthma. Previous studies have shown that 15%~18% of AR patients also have bronchial asthma.² Porter et al. collected information on annual live births between 1916 and 2016 and provided a prevalence of asthma ranging from 2.3 cases per 1000 individuals among the 1924 birth-year cohort to 29.8 cases per 1000 individuals among the 1990 birth-year cohort.¹⁹ Obviously, the number of people with asthma has increased rapidly. As early as 1984, Hopkirk reviewed the natural history of asthma in relation to aviation service and found that "asthma is incompatible with flying and aeromedical risk exceeded any potential benefits."¹⁰ Asthma and AR may occur sequentially or simultaneously. It is beneficial to manage asthma by controlling AR.

As early as in 1998, a report indicated a significant correlation between AR and chronic sinusitis in U.S. naval aircrew.²⁵ During descent while flying, the nasal mucosa is congested and swollen, especially in sufferers from AR, which leads to obstruction of the nasal sinus complex and leaves passengers and aircrew prone to aviation sinusitis. Another study of acute sinusitis compared Israeli air force pilots with ($N = 54$) and without AR ($N = 82$). Previous episodes of acute sinusitis were more common in the pilots with AR.²⁴ In our study, 421 cases presented with ear barotraumas and 404 cases with AR symptom aggravation during flight. Pressure in the middle ears changes through the Eustachian tube based on flight altitude. The mucosa of the Eustachian tube and middle ear are affected with edema with AR, which significantly increases the potential for ear barotraumas and aero-otitis media.

Table IV. Correlation of RQLQ or TNSS with Flight Time.

GROUPS ($N = 949$)	r_p	P
Total TNSS score - total flight time	0.130**	<0.001
Total TNSS score - flight time in last year	0.081**	<0.001
Total RQLQ score - total flight time	0.187**	<0.001
Total RQLQ score - flight time in last year	0.119**	<0.001

RQLQ: Rhino-conjunctivitis Quality of Life Questionnaire; TNSS: Total Nasal Symptoms Score; r_p : Spearman correlation coefficient.

** $P < 0.01$, indicating significantly correlated.

Severe AR not only causes nasal symptoms, but also leads to poor mental health, anxiety, depression, sleep disorders, and other problems, which can reduce patients' quality of life.^{7,8,14,28}

Sansone and Sansone found that 99.9% and 97.1%, respectively, of AR cases suffered from anxiety and depression.²¹ Allergies trigger the immune system to release cytokines, impair sleep through nasal obstruction, and secondarily exacerbate psychiatric symptoms. Additionally, allergies may negatively affect cognitive functioning and contribute to psychiatric disturbance.²¹ According to our study, seven sections of the RQLQ scale (activity, sleep, performance, practical problems, nasal symptoms, eye symptoms, and emotions) were significantly related to AR. Furthermore, practical problems, activities, and performance associated with AR are the top three troubles that compound distraction from flying duties. In daily health management of aircrew members, it is necessary to pay attention to symptoms and progression of AR, especially sleep, emotional, and psychological problems. In addition, scores from the RQLQ scale and the TNSS scale significantly correlated with total flight time and flight time in the last year, respectively. Also, total flight time was more closely correlated with RQLQ and TNSS, indicating that AR as a chronic disease course requires long-term standardized supervision and prevention.

In summary, this is the first report on prevalence of self-reported AR across various geographic regions in civil aviation aircrew in China. Duration and severity of AR symptoms vary for each aircrew, and can be controlled by medication, but cannot be cured completely at present. Those patients have a long treatment cycle and poor treatment compliance, which requires long-term health management. Through this study, we acquired a preliminary understanding of the current situation and complications of AR among civil aviation aircrew in China. This finding can help identify and assess potential risk factors to avoid and reduce the adverse impact of AR. We have a better understanding of the relationship between AR and related diseases and it is beneficial to the accurate medical treatment of AR and even whole airway diseases. In the long run, health management in aircrew with AR is of great significance to improve their quality of life and flying duties, which may provide a basis for defining new certification policies.

ACKNOWLEDGMENTS

The authors are grateful to all participants in this research as well as support from Shenzhen Airlines, Hebei Airlines, China Eastern Airlines, and China United Airlines.

Financial Disclosure Statement: This work was financially supported by Civil Flying Duties Capacity Fund (grant No. DFS20190601). The authors have no competing interests to declare.

Authors and affiliations: Yin Bai, M.D., Mosheng Hu, M.D., and Fengjie Ma, Ph.D., Civil Aviation Medical Assessment Institute, Civil Aviation Medicine Center, Civil Aviation Administration of China, Beijing, China; Ke Liu, B.D., Civil Aviation Medicine Center of Chengdu, Chengdu, Sichuan Province, China; Haijun Xu, B.D., Civil Aviation Medical Center of the Northeast Regional Administration, Shenyang, Liaoning Province, China; Xuan Wu, B.D.,

China Southern Airlines Co., Ltd., Xi'an, Shanxi Province, China; and Hongtiao Wang, Ph.D., Department of Allergy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China.

REFERENCES

- Biedermann T, Winther L, Till SJ, Panzner P, Knulst A, Valovirta E. Birch pollen allergy in Europe. *Allergy*. 2019; 74(7):1237–1248.
- Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision. *J Allergy Clin Immunol*. 2017; 140(4):950–958.
- Calais CJ, Robertson BD, Beakes DE. Association of allergy/immunology and obstructive sleep apnea. *Allergy Asthma Proc*. 2016; 37(6):443–449.
- Chiarella SE, Fernandez R, Avila PC. The genes and the environment in nasal allergy. *Curr Opin Allergy Clin Immunol*. 2015; 15(5):440–445.
- Chirakalwasan N, Ruxruntham K. The linkage of allergic rhinitis and obstructive sleep apnea. *Asian Pac J Allergy Immunol*. 2014; 32(4):276–286.
- Čosičkić A, Skokić F, Selimović A, Mulić M, Suljendić S, et al. Development of respiratory allergies, asthma and allergic rhinitis in children with atopic dermatitis. *Acta Clin Croat*. 2017; 56(2):308–317.
- El Hennawi DD, Ahmed MR, Farid AM. Psychological stress and its relationship with persistent allergic rhinitis. *Eur Arch Otorhinolaryngol*. 2016; 273(4):899–904.
- Flanigan C, Sheikh A, DunnGalvin A, Brew BK, Almqvist C, Nwaru BI. Prenatal maternal psychosocial stress and offspring's asthma and allergic disease: a systematic review and meta-analysis. *Clin Exp Allergy*. 2018; 48(4):403–414.
- Hernández CD, Casanello P, Harris PR, Castro-Rodríguez JA, Iturriaga C, et al. Early origins of allergy and asthma (ARIES): study protocol for a prospective prenatal birth cohort in Chile. *BMC Pediatr*. 2020; 20(1):164.
- Hopkirk JA. Natural history of asthma: aeromedical implications. *Aviat Space Environ Med*. 1984; 55(5):419–421.
- Huang Y, Wang C, Wang X, Zhang L, Lou H. Efficacy and safety of subcutaneous immunotherapy with house dust mites for allergic rhinitis: a meta-analysis of randomized controlled trials. *Allergy*. 2019; 74(1):189–192.
- Inal A, Kendirli SG, Yilmaz M, Altintas DU, Karakoc GB, Erdogan S. Indices of lower airway inflammation in children monosensitized to house dust mites after nasal allergen challenge. *Allergy*. 2008; 63(10):1345–1351.
- Khan SJ, Dharmage SC, Matheson MC, Gurrin LC. Is the atopic march related to confounding by genetics and early-life environment? A systematic review of sibship and twin data. *Allergy*. 2018; 73(1):17–28.
- Kim DH, Han K, Kim SW. Relationship between allergic rhinitis and mental health in the general Korean adult population. *Allergy Asthma Immunol Res*. 2016; 8(1):49–54.
- Meng Y, Wang C, Zhang L. Recent developments and highlights in allergic rhinitis. *Allergy*. 2019; 74(12):2320–2328.
- Noguchi E, Shibasaki M, Arinami T, Takeda K, Maki T, et al. Evidence for linkage asthma/atopy between in childhood and chromosome 5q31-q33 in a Japanese population. *Am J Respir Crit Care Med*. 1997; 156(5):1390–1393.
- Okubo K, Kurono Y, Ichimura K. Japanese guidelines for allergic rhinitis 2017. *Allergol Int*. 2017; 66(2):205–219.
- Pawankar R, Canonica GW, Holgate ST, Lockey RF, Blaiss MS, editors. *WAO White Book on Allergy: Update 2013*. 2013; [Accessed 2015-12-03]. Available from <http://www.worldallergy.org/UserFiles/file/WhiteBook2-2013-v8.pdf>.
- Porter WD, Powell-Dunford N, Wilde GD, Bushby AJR. Asthma and rotary-wing military aircrew selection. *Aerosp Med Hum Perform*. 2019; 90(7):606–612.
- Powell-Dunford N, Reese C, Bushby A, Munkeby BH, Coste S, et al. The aeromedical management of allergic rhinitis. *Aerosp Med Hum Perform*. 2018; 89(5):453–463.

21. Sansone RA, Sansone LA. Allergic rhinitis: relationships with anxiety and mood syndromes. *Innov Clin Neurosci*. 2011; 8(7):12–17.
22. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, et al. Clinical practice guideline: allergic rhinitis executive summary. *Otolaryngol Head Neck Surg*. 2015; 152(2):197–206.
23. Spielhauer M. Definition and clinic of the allergic rhinitis. *Med Monatsschr Pharm*. 2016; 39(3):97–99.
24. Ulanovski D, Barenboim E, Raveh E, Grossman A, Azaria B, Shpitzer T. Sinusitis in pilots of different aircraft types: is allergic rhinitis a predisposing factor? *Am J Rhinol*. 2008; 22(2):122–124.
25. Walker C, Williams H, Phelan J. Allergic rhinitis history as a predictor of other future disqualifying otorhinolaryngological defects. *Aviat Space Environ Med*. 1998; 69(10):952–956.
26. Wang W, Xian M, Xie Y, Zheng J, Li J. Aggravation of airway inflammation and hyper-responsiveness following nasal challenge with *Dermatophagoides pteronyssinus* in perennial allergic rhinitis without symptoms of asthma. *Allergy*. 2016; 71(3):378–386.
27. Wang XD, Zheng M, Lou HF, Wang CS, Zhang Y, et al. An increased prevalence of self-reported allergic rhinitis in major Chinese cities from 2005 to 2011. *Allergy*. 2016; 71(8):1170–1180.
28. Yang ZC, Tang BJ, Yu Y, Xin XH, Ma RX. [Efficacy analysis of psychological intervention on the basis of medication for the treatment of moderate-severe persistent allergic rhinitis]. [Article in Chinese]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2017; 31(21):1642–1645.
29. Zhang L, Han D, Huang D, Wu Y, Dong Z, et al. Prevalence of self-reported allergic rhinitis in eleven major cities in china. *Int Arch Allergy Immunol*. 2009; 149(1):47–57.
30. Zheng M, Wang X, Zhang L. Association between allergic and nonallergic rhinitis and obstructive sleep apnea. *Curr Opin Allergy Clin Immunol*. 2018; 18(1):16–25.