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The relationship between prebiotic intake and allergic rhinitis

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Abstract

Objectives: Exploring the relationship between intake of probiotics and the prevalence of allergic rhinitis.

Methods: Based on data from the National Health and Nutrition Examination Survey, dietary supplement labels were examined to identify products containing probiotics and prebiotics. Statistical methods were used to analyze the factors influencing the prevalence of allergic rhinitis, and further stratified analysis was conducted to control for confounding factors.

Results: The proportion of individuals not consuming probiotics was significantly higher in the allergic rhinitis (AR) group than in those consuming them, suggesting a correlation between probiotics and AR. In the male subgroup with probiotic intake, the adjusted odds ratio (95% confidence interval) was 0.28 (0.10–0.75), $p = .02$, indicating that probiotic intake was a protective factor for AR in the male population. In the probiotic-intake group, the odds ratio for age < 65 was 0.26 (0.07–0.94), $p = .04$, and for age ≥ 80 was less than 1 with $p < .0001$, suggesting that probiotic intake was a protective factor for AR in age < 65 and age ≥ 80 populations, both with statistical significance.

Conclusion: Intake of probiotics is associated with a reduced prevalence of allergic rhinitis, particularly in the male population and individuals aged <65 years and ≥ 80 years.

Level of Evidence: Level 4.

KEYWORDS
allergic rhinitis, gut microbiota, probiotics

1 | INTRODUCTION

Allergic rhinitis (AR), a chronic upper respiratory tract disease, is one of the most common diseases globally and typically lasts a lifetime.[1,2] It is estimated to affect 10%–30% of the world's population, causing enormous economic and medical burdens. AR is a noninfectious inflammatory disease of the nasal mucosa mediated by immunoglobulin E (IgE) following exposure to allergens and involves various immune-active cells and cytokines.[3] Typical symptoms of AR include nasal congestion, itching, rhinorrhea, and sneezing.[4] Indoor dust mites, animals, and mold spores are the primary triggers for year-round symptoms, while seasonal or intermittent symptoms are usually

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caused by contact with pollen. Complete avoidance of common environmental allergens causing AR is not feasible, and treatment options usually focus on symptom relief. Drug therapy mainly includes antihistamines, steroids, and allergen removal methods, while immunotherapy involves injecting small doses of allergens to induce immune tolerance and relieve AR symptoms. These treatment methods only provide short-term relief of symptoms, and some AR patients may not respond well to treatment, highlighting the need for further exploration of the pathogenesis and treatment strategies for AR.

The gut microbiota plays a vital role in the development and regulation of local and systemic immunity, and abnormal gut microbiota composition has been associated with some immune-mediated diseases, including allergic diseases. In recent years, the relationship between gut microbiota and AR has drawn wide attention. Studies have shown that gut microbiota dysbiosis is associated with immune-mediated diseases and may cause immune system dysregulation, thereby promoting the occurrence of AR.[5–7] Over the past few decades, there has been a significant increase in the prevalence of allergic diseases such as asthma, eczema, food allergies, and AR worldwide. The hygiene hypothesis suggests that this increase is related to reduced early-life exposure to microorganisms, leading to abnormal gut microbiota composition and subsequent immune dysfunction.[8]

Probiotics are defined as microorganisms that exist within a host in specific forms and in sufficient quantities to provide health benefits to the host.[9] Currently, probiotics used for disease treatment mainly include lactobacillus, such as cheese lactobacillus, short lactobacillus, and *Lactobacillus rhamnosus*, as well as bifidobacterium, such as *Bifidobacterium breve* and *Bifidobacterium thermophilum*.[10–13] Probiotics mainly exist in the human digestive tract, which is both the organ with the richest bacteria in terms of quantity and variety as well as one of the most important immune organs in the human body, and 70% of the immune system is located in the intestine.[14] The role of probiotics in the gastrointestinal tract is to help degrade or alter antigens in the intestine, maintain the normal microbial population in the intestine, regulate the secretion of pro-inflammatory factors, and establish the immune system. The role of probiotics in shaping the immune system is particularly evident in the early stages of life.

Prebiotics are a type of nutritional supplement that is typically an indigestible dietary fiber compound designed to promote bacterial growth and function. Prebiotics may alter early-life immune development.[7] Diets rich in fiber and oligosaccharides may increase the amount of short-chain fatty acids in the intestine, which has beneficial effects on immunity and longevity.[15] Prebiotics have a regulating effect on the intestinal microbiome and may have potential preventive and therapeutic effects on the pathogenesis of AR. Studies have shown that prebiotics can improve intestinal barrier function and reduce abnormal immune system reactions by regulating the intestinal microbiome, increasing the proportion of beneficial bacterial communities, and reducing the proportion of harmful bacterial communities.

In summary, AR is a common allergic disease whose pathogenesis is mainly related to abnormal immune system reactions. Currently, drug therapy and immunotherapy are commonly used treatment methods. The correlation between the intestinal microbiome and AR is also worth considering. Prebiotics may have potential roles in the prevention and treatment of AR, but more research is needed to confirm this.

2 | MATERIALS AND METHODS

Conducted by the Centers for Disease Control and Prevention, National Health and Nutrition Examination Survey (NHANES) is a cross-sectional nationwide survey designed to assess the health and nutrition status of children and adults in the United States. Demographic, dietary, and health-related queries are collected via interviews, physiologic measurements, and laboratory tests administered by trained personnel. Participants are selected through a stratified multistage probability design to provide a representative sample of the US population. Detailed descriptions are available online.[16]

This study was designed as a cross-sectional study on patients with AR using data from the NHANES. This database was regularly updated and a nationally representative sample of about 5000 persons was examined each year. This analysis included 87,174 patients with AR (ages ≥18). Then, we obtained participant information on demographic characteristics, health-related lifestyle, and complicated diseases. Then these data were used to assess the association between prebiotic intake and the risk of AR.

We selected the subjects Based on data from the NHANES according to the process shown in Figure 1. The data of AR were extracted by reference to previous literature.[17,18] The AR data were derived from questionnaire data, respondents are diagnosed with AR based on an affirmative response to three survey questions: "Do you get symptoms such as sneezing, runny nose, or itchy or watery eyes due to hay fever, seasonal, or year-round allergies?" and "Have you ever been told by a doctor or other health professional that you had hay fever, seasonal, or year-round allergies?" and "Episode of hay fever in past 12 months?"

2.1 | The definition of prebiotics

Prebiotics are a type of dietary fiber supplement that selectively stimulates the growth and activity of bacteria in one or a few colonies to produce beneficial effects on the host's health and are indigestible food components. We divided AR patients into two groups according to their prebiotic intake: non-prebiotic users and prebiotic users. We extract prebiotic metadata data by referring to previous literature.[19,20] Prebiotic data were derived from telephone dietary recall, and prebiotic consumption was assessed using the first day of the dietary interview (a 24-h dietary recall interview before the survey) and the second day of the dietary interview (a second 24-h dietary recall interview collected by telephone 3–10 days after the first interview). Specifically, the prebiotics was identified by text mining key phrases, including the names and ingredients of dietary supplements, as well as the names and ingredients of drugs, including "acadia gum," "chicor," "glucan," "gum arabic," "inulin," "lactulose," "oligofruc," "oligosac,"

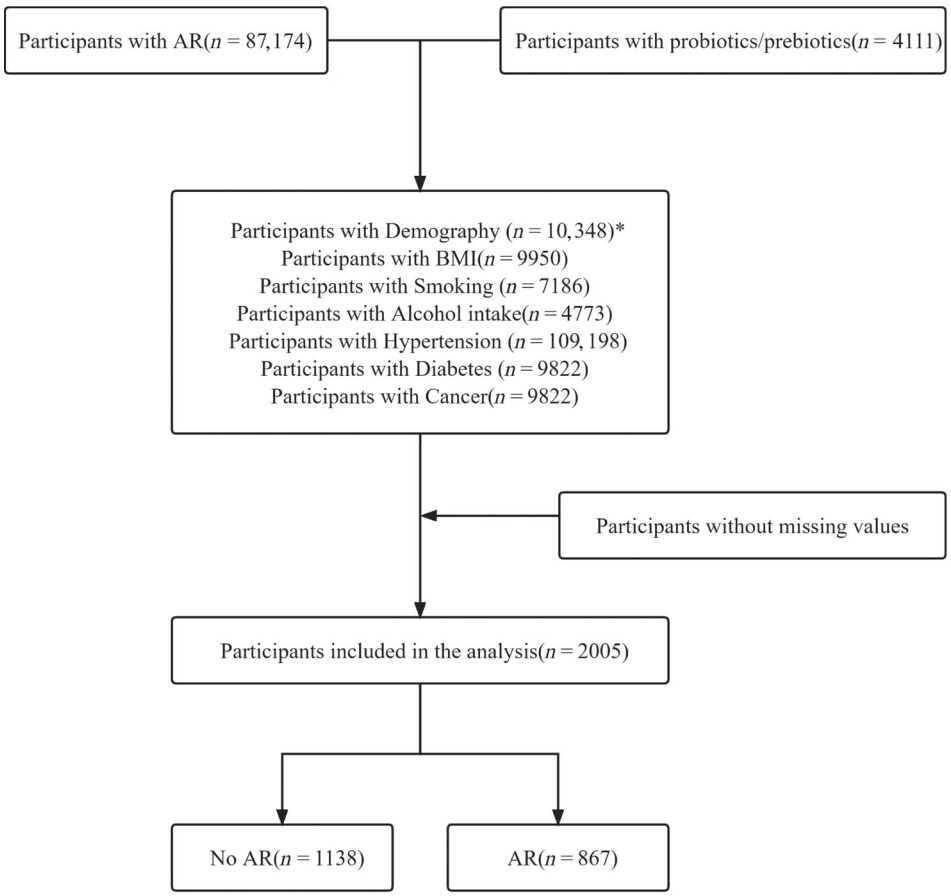

FIGURE 1 Participants included in statistical analysis based on baseline population characteristics.

"polcydextrose," "prebiotic," "pre-biotic," "prebiotoc," "psyllium," "pesistant starch," and "wheat dextrin."

2.2 | Definition of alcohol users and smokers

According to previous reports,[21] drinkers were divided into non-drinkers, former drinkers, light drinkers (<2 drinks per day for females, <3 drinks per day for males, or binge drinking <2 days per month), moderate drinkers (≥2 drinks per day for females, ≥3 drinks per day for males, or binge drinking ≥2 days per month), and heavy drinkers (≥3 drinks per day for females, ≥4 drinks per day for males, or binge drinking [≥4 drinks on same occasion for females, ≥5 drinks on same occasion for males] on 5 or more days per month).

Smoking status was divided into nonsmokers, former smokers, and current smokers. Current smokers were defined as those who currently smoke every day or some days. Former smokers were confirmed to have smoked at least 100 cigarettes in their lifetime but do not currently smoke.[22]

2.3 | Statistical analysis

Continuous variables were expressed as mean and standard deviation, and categorical variables were expressed as numbers or percentages. Demographic characteristics included age, sex, race (white, black, Mexican, etc.), and body mass index (BMI), listed in Table 1. We used adjusted binary logistic regression models to evaluate the relationship between prebiotic intake and the incidence of AR, expressed as the odds ratio (OR) and 95% confidence interval (95% CI). In the multivariate-adjusted model, potential risk factors for AR were age, sex, smoking status, alcohol consumption, BMI (BMI < 25.0 kg/m^2, BMI≥25.0 kg/m^2), hypertension (none, hypertension), and diabetes (none, diabetes). Then, several adjusted models were performed: Model 1 (adjusted for age), Model 2 (adjusted for age, sex, and race), and Model 3 (Model 2 plus adjustment for smoking status, alcohol consumption, BMI, hypertension, and diabetes), listed as in Table 2.

3 | RESULTS

Table 1 shows that the average age of the study population with AR was 46.78 ± 0.91 years old, while the average age of the population without AR was 48.24 ± 0.73 years old. The overall average age was 47.56 ± 0.71 years old. Compared to the nonallergic rhinitis (NAR) group, the AR group was more likely to be composed of individuals who did not consume probiotics. Specifically, the AR group had a significantly greater proportion of individuals who did not consume probiotics compared to those who did consume probiotics. This suggests

TABLE 1 Demographic characteristics of the study population.

Variable	Total	No AR	AR	*p*-value
BMI(body mass index)	28.40(0.26)	28.50(0.27)	28.29(0.32)	.5
Age	47.56(0.71)	48.24(0.73)	46.78(0.91)	.09
Poverty	3.48(0.06)	3.52(0.06)	3.42(0.07)	.17
Prebiotic				.03
No	5126743.85	95.85	98.27	
Yes	159849.63	4.15	1.73	
Probiotic				.74
No	5133096.81	97.27	96.90	
Yes	153496.67	2.73	3.10	
Alcohol user				.14
Never	453448.99	7.85	9.41	
Former	841529.29	18.13	13.38	
Mild	1967722.81	35.97	38.66	
Moderate	1003124.37	18.18	19.89	
Heavy	1020768.01	19.87	18.67	
Race				.01
White	4241388.28	82.98	77.07	
Mexican	224167.66	3.54	5.04	
Black	387680.75	5.03	9.98	
Other	433356.80	8.45	7.91	
Marital status				.01
Married	3306555.06	65.91	58.68	
Widowed	243734.60	5.07	4.09	
Divorced	606983.48	10.08	13.10	
Separated	110435.26	1.62	2.62	
Never married	631743.55	9.59	14.66	
Living with partner	387141.52	7.73	6.85	
Education				.12
Under high school	554159.48	11.72	9.06	
High school or equivalent	1245332.65	24.38	22.61	
Above high school	3487101.35	63.90	68.33	
Diabetes				.27
No	4921878.90	93.81	92.28	
Yes	364714.59	6.19	7.72	
Hypertension				.49
No	3331721.99	63.82	62.10	
Yes	1954871.49	36.18	37.90	
Smoking status				.01
Never	2684620.07	46.58	55.60	
Former	1460473.77	29.11	25.92	
Now	1141499.64	24.30	18.48	
Sex				.05
Male	2559070.98	45.97	51.21	
Female	2727522.50	54.03	48.79	
Cancer				.47
No	4871592.73	92.62	91.61	
Yes	415000.75	7.38	8.39	

TABLE 2 Multivariable-adjusted odds ratio (95% confidence intervals) of allergic rhinitis (AR) by consumption of prebiotic.

		No prebiotics consumption	Prebiotics consumption Model 1[a]		Model 2[b]		Model 3[c]	
			OR	*p*	OR	*p*	OR	*p*
All			0.41(0.18, 0.94)	.04	0.42(0.18, 0.98)	.049	0.39(0.17, 0.90)	.03
Sex	Male	Ref	0.30(0.10, 0.91)	.04	0.31(0.11, 0.93)	.04	0.28(0.10, 0.75)	.02
	Female	Ref	0.54(0.18, 1.57)	.23	0.51(0.17, 1.51)	.2	0.45(0.14, 1.40)	.16
BMI (body mass index)	Normal	Ref	0.26(0.06, 1.09)	.06	0.27(0.06, 1.24)	.09	0.22(0.05, 0.92)	.04
	Low	Ref	0.98(0.38, 2.53)	.96	0.99(0.37, 2.65)	.98	0.86(0.35, 2.15)	.74
	High	Ref	0.22(0.05, 0.97)	.049	0.22(0.05, 0.98)	.049	0.22(0.04, 1.21)	.08
Age	= < 65	Ref	0.27(0.08, 0.98)	.05	0.27(0.07, 1.01)	.05	0.26(0.07, 0.94)	.04
	65 – 80	Ref	1.26(0.37, 4.24)	.69	1.27(0.38, 4.19)	.67	1.41(0.36, 5.45)	.6
	> = 80	Ref	0.00(0.00, 0.00)	<.0001	0.00(0.00, 0.00)	<.0001	0.00(0.00, 0.000000e+00)	<.0001
Alcohol user	Never	Ref	0.23(0.04, 1.36)	.1	0.21(0.04, 1.27)	.08	0.13(0.03, 0.68)	.02
	Former	Ref	0.44(0.08, 2.36)	.31	0.41(0.08, 2.25)	.27	0.33(0.08, 1.41)	.13
	Mild	Ref	0.47(0.17, 1.32)	.14	0.48(0.16, 1.44)	.17	0.42(0.14, 1.24)	.11
	Moderate	Ref	0.85(0.09, 8.41)	.88	0.86(0.06, 12.32)	.9	0.71(0.02, 21.81)	.83
	Heavy	Ref	0.23(0.04, 1.33)	.09	0.22(0.03, 1.56)	.12	0.21(0.04, 1.16)	.07
Race	White	Ref	0.41(0.17, 0.99)	.049	0.42(0.18, 1.02)	.06	0.38(0.16, 0.93)	.03
	Mexican	Ref	0.35(0.02, 5.64)	.42	0.40(0.02, 6.98)	.46	0.35(0.03, 4.66)	.39
	Black	Ref	0.16(0.01, 2.92)	.19	0.18(0.01, 4.16)	.25	0.14(0.01, 2.91)	.18
	Other	Ref	0.88(0.06, 13.01)	.92	0.87(0.06,12.88)	.91	1.38(0.18, 10.53)	.74
Smoking status	Never	Ref	0.37(0.16, 0.88)	.03	0.39(0.17, 0.91)	.03	0.38(0.14, 1.05)	.06
	Former	Ref	0.49(0.13, 1.89)	.28	0.49(0.12, 2.08)	.3	0.46(0.12, 1.72)	.23
	Now	Ref	0.11(0.00, 3.26)	.18	0.10(0.00, 2.91)	.16	0.10(0.00, 2.70)	.16
Diabetes	No	Ref	0.37(0.15, 0.87)	.03	0.38(0.16, 0.89)	.03	0.34(0.14, 0.80)	.02
	Yes	Ref	0.68(0.09, 5.27)	.69	0.73(0.09,6.12)	.75	0.87(0.09, 8.08)	.89
Hypertension	No	Ref	0.41(0.15, 1.10)	.07	0.42(0.14, 1.26)	.11	0.43(0.15, 1.18)	.09
	Yes	Ref	0.40(0.09, 1.69)	.19	0.39(0.09, 1.77)	.2	0.29(0.06, 1.47)	.13

[a]Model 1 (adjusted for age).
[b]Model 2 (adjusted for age, sex, and race).
[c]Model 3 (Model 2 plus adjustment for smoking status, alcohol user, BMI, hypertension, and diabetes).

a potential correlation between probiotic intake and AR. Additionally, the population with AR was more likely to be male, white, and married and less likely to smoke.

The relationship between probiotic intake and the incidence of AR is shown in Table 2. The age-adjusted OR (95% CI) was 0.41 (0.18–0.94). The multivariate-adjusted OR (95% CI) was 0.42 (0.18–0.98). Further adjustment for hypertension, diabetes, and lifestyle factors (smoking and alcohol intake) revealed an even more significant difference between the probiotic intake group and the non-probiotic intake group.

We conducted stratified analyses based on population characteristics, including gender, race, age, BMI, hypertension, smoking, alcohol intake, and diabetes, to analyze the correlation between probiotic intake and the incidence of AR. Smoking and hypertension were not likely to significantly alter this correlation. However, significant changes in the correlation between probiotic intake and AR incidence were observed for race, BMI, gender, age, diabetes status, and alcohol intake. Specifically, in the male population, the multivariate OR (95% CI) was 0.28 (0.10–0.75), $P = 0.02$, suggesting that probiotic intake is a protective factor for AR in males. Additionally, we found a significant correlation between probiotic intake and AR incidence for individuals under the age of 65 and those over the age of 80, but not for those between the ages of 65 and 80. In the probiotic intake group, the OR for individuals under the age of 65 was 0.26 (0.07–0.94), $P = 0.04$, and the OR for individuals over the age of 80 was less than 1 ($P < 0.0001$), both of which were statistically significant, suggesting that probiotic intake is a protective factor for AR in individuals under 65 years old and those over 80 years old.

4 | DISCUSSION

Previous studies have shown a causal relationship between gut microbiota and allergic diseases, as gut microbial dysbiosis can lead to abnormal immune reactions and promote the development of AR.[5,6] Prebiotics can regulate gut dysbiosis,[23] providing a new therapeutic approach for indirectly affecting the progression of AR by modulating the gut microenvironment through prebiotic intake. The advantage of prebiotics lies in their selective fermentation by bifidobacteria or lactobacilli, dependent on stimulating the host's own bifidobacteria or lactobacilli populations. Prebiotics escape digestion and absorption in the upper gastrointestinal tract, arrive intact in the colon, and are fermented by a limited number of bifidobacteria and lactobacilli.[24] The data from this study suggest that the majority of individuals in the AR group did not consume prebiotics compared to the NAR group, and there was a statistically significant difference. This indicates that prebiotics may be related to AR, and further stratified analysis of confounding factors reveals that prebiotics can indeed play a role in the intervention or treatment of AR for certain specific populations, such as those without diabetes. This study's data show that prebiotic intake is a protective factor for AR patients without diabetes, and prebiotic intake reduces the risk of AR by 66% in individuals without diabetes compared to those who do not consume prebiotics. Previous reports have shown that gut dysbiosis directly promotes the development of type 1 and type 2 diabetes.[25] Therefore, the profound effect of gut dysbiosis may influence the efficiency of microbial supplements in AR patients with diabetes complications. In the gender-stratified analysis, probiotic intake is a protective factor for AR in males, prebiotics especially affect IgE-associated diseases is also supported by the observation that boys benefited from the treatment more than did girls; the boys' total IgE level was also higher. Compared with girls, boys more frequently produce IgE antibodies.[26–29] In the age-stratified analysis, we found that prebiotic intake is a protective factor for AR in populations under 65 and over 80 years old, as factors such as gut dysbiosis correlate with the development of pathological conditions. These factors include an imbalanced diet, environmental toxins, drugs, ROS, psychological stress, and other pro-inflammatory factors. For example, gut dysbiosis caused by antibiotic use, and high-fat or carbohydrate intake is associated with obesity and metabolic disorders. The gut barrier is the primary site of interaction between microorganisms, nutrients, and the immune system. It consists of intestinal epithelial cells (IECs) and the mucosal layer, which protect the body from harmful compounds and pathogens while allowing selective nutrient absorption. Cytokine production is a major characteristic of IECs, affecting the activity of mucosal dendritic cells and T regulatory cells. Gut health depends on the cross-talk between the microbiota and the immune system.[30] As age increases, the production of pro-inflammatory cytokines such as IL-6 increases.[31] Age-related factors such as dysbiosis disrupt the host's immune system, and changes in dietary habits result in barrier dysfunction.[32] For individuals over 80 years old, aging leads to gut microbial dysbiosis, and prebiotics are rich in dietary fiber. Prebiotic intake increases dietary fiber content and thus affects the gut microbiota, increasing the circulating level of short-chain fatty acids. Short-chain fatty acids, mainly acetate, butyrate, and propionate, are microbial metabolites produced by the fermentation of partially and/or undigested polysaccharides. For example, propionate enhances bone marrow hematopoietic function and exhibits the ability to activate TH2 effect cells in respiratory organs, thereby preventing sustained and rapid clearance of allergic airway inflammation.[15] Short-chain fatty acids have antimicrobial activity and promote homeostasis by participating in maintaining colonic epithelial integrity, metabolism, and immune function.[33,34] Short-chain fatty acids are not only an energy source for the gut microbiota itself but also IECs' energy source. Regulating the gut microbiota is an attractive way to restore the gut barrier integrity and immune system in the elderly.[35] Since Gibson and Roberfroid introduced prebiotics in 1995, they have become increasingly popular and have provided theoretical support for selectively regulating the gut microbiota, producing short-chain fatty acids, and enhancing immune function.[24,32] For populations under 65 years of age, long-term imbalanced diets, overuse of antibiotics, or other pathological factors can also lead to gut dysbiosis, and prebiotic intake can have an intervention effect on AR. These associations provide a new direction for future treatment and prevention of AR. With the increasing global prevalence of AR, AR patients are suffering, severely affecting their daily work, life, socializing, and sleep quality. Traditional treatment options have shown unsatisfactory results, and further research on AR is necessary to seek better treatment options. One limitation of this study is the lack of in-depth research on the relationship between prebiotics intake and the incidence of AR, such as the dosage, timing, and types of prebiotics intake and their effects on the incidence of AR. These factors may provide insights and possibilities for future research in this area. In addition, the inclusion criteria for people with AR in this study had certain limitations. Although we identified AR patients based on the answers to the three survey questions by referring to previous literature,[17,18] the diagnosis of AR required a positive test accompanied by related symptoms, which may lead to the risk of deviation of the included population.

5 | CONCLUSION

AR is one of the most common allergic diseases, can lead to nasal congestion, runny nose, nose itching, and sneezing, having a serious impact on the quality of daily life, at present, drug therapy and immunotherapy are the most commonly used treatment, but the treatment effect is not satisfactory. This study suggests that the intake of prebiotics can regulate the gut microbiota and improve gut dysbiosis, thereby playing a therapeutic role in AR. particularly in the male population and individuals aged <65 years and ≥80 years. This study provides a new therapeutic direction for patients with AR.

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CONFLICT OF INTEREST STATEMENT

Chao Chang, Qiuyang Wang, Xiaodan Li, Huazhang Tan, and Guoxin Huang declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets analyzed are publicly available summary statistics in this study.

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