Early risk and protective factors for allergic rhinitis in children: A cross-sectional study

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Abstract

Background: Allergic rhinitis (AR) is one of the most common inflammatory diseases, leading to health and economic burdens. Genetic and environmental factors may influence the development of AR in early life. **Materials and methods:** A cross-sectional study was conducted with 320 pediatric patients from the Department of Otorhinolaryngology - Ophthalmology - Maxillofacial Surgery, the Department of Pediatrics at Hue University of Medicine and Pharmacy Hospital, and the Pediatric Center of Hue Central Hospital between April 2022 and December 2023. Data on allergies, clinical history, family background, and environmental factors were collected through a parent-reported survey based on the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Logistic regression analysis was used to estimate the odds ratios (OR) for potential factors contributing to AR. **Results**: The proportion of children with current AR was 29% in the 6-7-year-old group, 26.2% in the 13-14-year-old group, and 28.1% across all groups. Parental allergy (adjusted OR 2.44, 95% confidence interval [CI] 1.28-4.66), maternal age (1.85, 1.05-3.26), and history of eczema (1.95, 1.06-3.59) were independently associated with increased risks of AR. In stratified analyses, there was evidence that prolonged breastfeeding ≥12 months and dog exposure decreased the risk of AR in the 6-7-year-old group. **Conclusions**: Certain environmental and genetic factors were associated with AR in children aged 6-7 and 13-14 within a small contemporary pediatric outpatient cohort. However, a large-scale study is needed to validate these findings.

***Keywords**: Allergic rhinitis, early childhood, lifestyle, environment factors, hygiene hypothesis, microbial dispersal.*

1. INTRODUCTION

Allergic rhinitis (AR) is a long-term inflammatory condition of the nose that occurs when the immune system has an exaggerated response to airborne allergens, leading to an IgE-mediated reaction. Symptoms of AR include a runny or congested nose, sneezing, red and itchy eyes, watery eyes, and swelling around the eyes [1]. The prevalence of AR varies between children and adults, with around 25% of children and up to 40% of adults affected.

In Europe, the prevalence among adults ranges from 17% to 28.5% [2], while in Vietnam, approximately 20% of the population suffers from this condition [3].

The development of AR is strongly associated with the early childhood period when children encounter various risk and protective factors. At the same time, the gut microbiome remains unsettled until it reaches a stable phase between 31 and 46 months of age [4]. In addition to the microbiome, a range of lifestyle factors and environmental exposures contribute to the development of AR by the hygiene hypothesis [5].

Numerous studies worldwide have investigated factors associated with AR. However, even longitudinal studies focusing on early childhood risk factors for AR have yielded inconsistent and varying results. While some risk and protective factors have been consistently identified, others remain controversial. These discrepancies can be attributed to geography, ethnicity, study design, and the studied populations. Nonetheless, we are keen on exploring additional risk factors to gain a deeper understanding of the pathogenesis of AR [6]. Therefore, we conducted this study to identify some AR-related factors in our region.

2. MATERIALS AND METHODS

Study design

This was a multi-center and descriptive cross-sectional study.

Participants

Children aged 6-7 and 13-14 who visited the Department of Otorhinolaryngology - Ophthalmology - Maxillofacial Surgery, the Department of Pediatrics at Hue University of Medicine and Pharmacy Hospital,

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and the Pediatric Center of Hue Central Hospital between April 2023 and December 2023 were invited to participate in the study. The study received approval from the Human Research Ethics Committee of Hue University of Medicine and Pharmacy Hospital and the Human Research Ethics Committee of Hue Central Hospital. Informed consent/assent was obtained from the children 's parents.

Exclusion criteria: Pediatric patients or their parents (for younger children) who could not communicate or speak Vietnamese clearly.

Vietnamese ISAAC questionnaire

A survey was carried out using the parent-reported ISAAC (International Study of Asthma and Allergies in Childhood) questionnaire, which had been translated into Vietnamese and validated for two age groups: 6-7 years and 13-14 years [3]. Demographic questions included the participant's name, age, date of birth, hospital (for adolescents and children), sex, and interview date. Each questionnaire was coded with a unique number specific to each hospital center and participant, ensuring confidentiality and enabling the linkage of questionnaires between adults and children. The Vietnamese version of the ISAAC questionnaire included questions on doctor-diagnosed asthma, rhinitis, and eczema. These core questions were sensitive and specific, demonstrating good content, construct, concurrent, and predictive validity. The questionnaire on microbial dispersion factors, environment, and lifestyle in the early stages of life, developed for ISAAC phase III, was expanded for use in this study.

Definition of AR, severe AR, and rhinitis

The standardized core symptom questionnaire, identical to the one used in ISAAC phase I, included five questions about rhinitis or rhinoconjunctivitis symptoms. These questions were as follows:

1. Has your child ever had a problem with sneezing or a runny or blocked nose when he or she DID NOT have a cold or "the flu"?

2. In the past 12 months, has your child had a problem with sneezing or a runny or blocked nose when he or she DID NOT have a cold or "the flu"?

3. In the past 12 months, has this nose problem been accompanied by itchy/watery eyes?

4. In which of the past 12 months did this nose problem occur? (Month names listed)

5. In the past 12 months, how much did this nose problem interfere with your child's daily activities? (Not at all, a little, a moderate amount, a lot)

Because there is no appropriate Vietnamese equivalent for "hay fever," the question regarding this condition was excluded from our questionnaire.

Question 2 was utilized to estimate the prevalence of current rhinitis, and question 3 was used to estimate the prevalence of current conjunctivitis. Questions 2 and 3 were combined to evaluate current rhinoconjunctivitis (ACR) symptoms or current AR. Questions 2 and 3, along with the answer "A LOT" to question 5, were used to determine the prevalence of severe rhinoconjunctivitis symptoms or severe AR [7].

Data processing and analysis:

Statistical analyses were performed using STATA software (Stata 18 for Windows, StataCorp LP, College Station, TX, USA). Ordinal variables were described using absolute frequencies and percentages with 95% confidence intervals (95% CI). Necessary statistical tests: Chi-square test, Fisher's exact test, and multivariable logistic regression are performed with variables with p-value < 0.1 in univariate analysis. The relationship between AR and risk and protective factors was presented as adjusted Odds ratios (OR) and 95% CI.

3. RESULTS

The study included 320 participants, and Table 1 presents the prevalence of rhinitis symptoms based on age group. Among children aged 6-7 years, the prevalence of current rhinitis was 46.1% (95% CI: 39.5-52.8%), while in those aged 13-14 years, it was 38.8% (95% CI: 29.8-48.7%). Overall, the prevalence of current rhinitis across all children was 43.8% (95% CI: 38.4-49.3%).

Table 1. Prevalence of questionnaires-based condition of rhinitis

Conditions	All (n=320)		6-7 years (n=217)		13-14 years (n=103)	
	N	Prevalence (95% CI)	N	Prevalence (95% CI)	N	Prevalence (95% CI)
Current AR or ARC	90	28.1 (23.5, 33.3)	63	29.0 (23.4, 35.5)	27	26.2 (18.6, 35.7)
Current rhinitis	140	43.8 (38.4, 49,3)	100	46.1 (39.5, 52.8)	40	38.8 (29.8, 48.7)
Severe AR	12	3.8 (2.1, 6.5)	7	3.3 (1.5, 6.6)	5	4.9 (2.0, 11.2)

Abbreviation: AR, allergic rhinitis; ARC, allergic rhinoconjunctivitis

Current AR or ARC - the answer "YES" to question number 2 and 3

Current rhinitis - the answer "YES" to question number 2

Severe AR - the answer "YES" to question number 2 and 3 and the answer "A LOT" to question number 5

For AR, the prevalence was 29.0% (95% CI: 23.4-35.5%) in children aged 6-7 years and 26.2% (95% CI: 18.6-35.7%) in those aged 13-14. The overall prevalence of current AR in all children was 28.1% (95% CI: 23.5-33.3%).

In our area, the patterns of rhinitis symptoms in children were predominantly perennial. The prevalence of severe allergic rhinitis (AR) in children aged 6-7 years was 3.3% (95% CI: 1.5-6.6%), while in those aged 13-14 years, it was 4.9% (95% CI: 2.0-11.2%). Overall, the prevalence of severe AR in all children was 3.8% (95% CI: 2.1-6.5%). There was an association with another allergic disease: 36.7% of children with AR had eczema.

A parental history of atopy was significantly related to current AR (p<0.01, OR = 2.39, 95%CI = 1.24-4.61). Gestational age from 24 to 35 years was associated with current AR (p = 0.03, OR = 1.86, 95%CI = 1.05-3.28). Diagnosed eczema was related to current AR (p = 0.04, OR = 1.92, 95%CI = 1.04-3.56) (Tables 2 and 3, Figure 1).

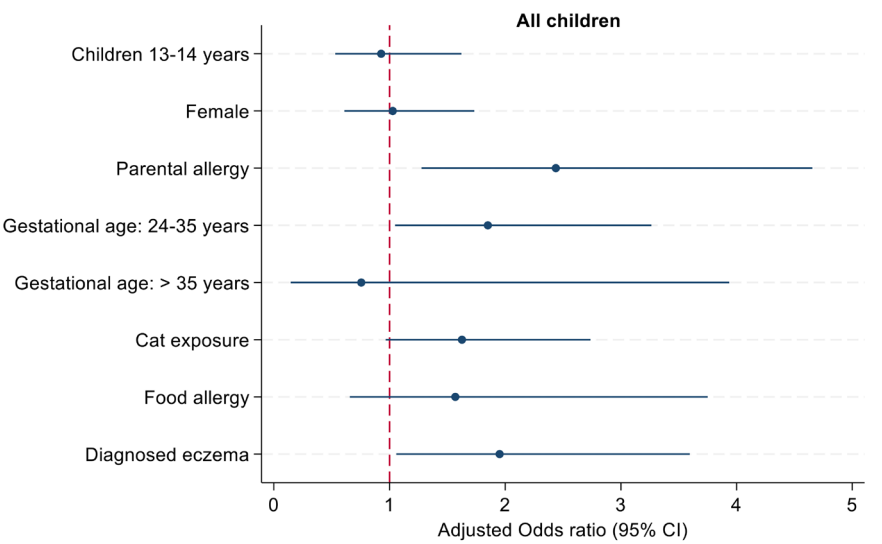

Figure 1. Risk of AR and potential factors in multiple logistic regression model of all children

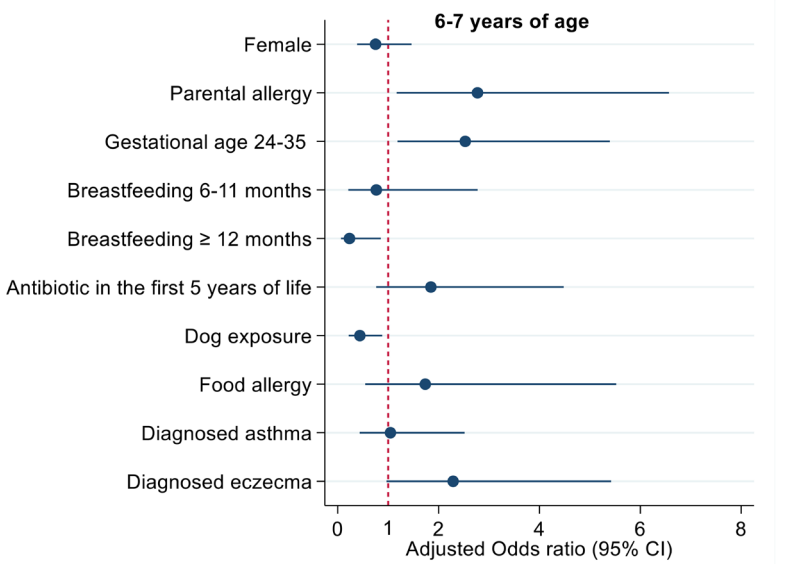

Figure 2. Risk of AR and potential factors in multiple logistic regression model of 6-7-year children

Concerning the age group of 6-7 years, parental history of allergy was significantly related to current AR (p=0.04, OR=2.47, 95%CI=1.06-5.78). Gestational age from 24 to 35 years was positively associated with current AR (p=0.02, OR=2.53, 95%CI=1.19-5.39). Antibiotics in the first year of life were associated with increased current AR (p=0.02, OR=2.56, 95%CI=1.17-6.61). However, the effect did not remain in the multiple logistic regression (p=0.18, OR=1.85, 95%CI=0.76-4.48). Parental reported breastfeeding (>12 months) was positively associated with decreased risk current AR (p = 0.03, OR=0.23, 95%CI=0.06-0.85). Current dog exposure was also associated with decreased risk of current AR (p=0.02, OR=0.44, 95%CI=0.22-0.88), as shown in Tables 2 and 3 and Figure 2.

In the children aged 13-14, parental history of atopy was not significantly related to an increased risk of current AR (p=0.18, OR=2.07, 95%CI=0.71-6.04). Diagnosed eczema was associated with current AR (p<0.01, OR=4.26, 95%CI=1.44-12.60) (Tables 2 and 3).

Table 2. Characteristic of children categorized by age group

Factors		**All (n=320)**			**6-7 years (n=217)**			**13-14 years (n=103)**		
		N	**n (%)**	**P**	**N**	**n (%)**	**P**	**N**	**n (%)**	**P**
Age (year)	6-7	217	63 (29.0)	0.60	-	-	-	-	-	-
	13-14	103	27 (26.2)		-	-	-	-	-	-
Sex	Male	157	43 (28.8)	0.77	99	31 (31.3)	0.50	58	12 (20.7)	0.15
	Female	163	47 (27.4)		118	32 (27.1)		45	15 (33.3)	
Parental allergy	No	265	64 (24.2)	<0.01	180	44 (24.4)	<0.01	85	20 (23.5)	0.18
	Yes	55	26 (47.3)		37	19 (51.4)		18	7 (38.9)	
Living place	Rural	208	59 (28.4)	0.90	147	44 (29.9)	0.67	61	15 (24.6)	0.65
	Urban	112	31 (27.7)		70	19 (27.1)		42	12 (28.6)	
Truck traffic	Never	12	3 (25,0)	0.97	9	2 (22.2)	0.90	3	1 (50.0)	0.85
	Sometime	173	49 (28.3)		119	36 (30.3)		54	13 (24.1)	
	Always	135	38 (28.1)		89	25 (28.1)		46	13 (28.3)	
Birth delivery	VD	228	62 (27.2)	0.56	151	42 (27.8)	0.55	77	20 (26.0)	0.92
	CS	92	28 (30.4)		66	21 (31.8)		26	7 (26.9)	
Gestational age	≤24	115	25 (21.7)	0.11	77	14 (18.2)	0.01	38	11 (28.9)	0.71
	24-35	194	63 (32.5)		135	49 (36.3)		59	14 (23.7)	
	≥35	11	2 (18.2)		5	0 (0.0)		6	2 (33.3)	
Smoking during pregnancy	No	-	-	-	102	25 (24.5)	0.27	-	-	-
	Passive MS	-	-	-	113	37 (32.7)		-	-	-
	Active MS	-	-	-	2	1 (50.0)		-	-	-
Birthweight	≤2500 g	-	-	-	27	9 (33.3)	0.60	-	-	-
	>2500 g	-	-	-	190	54 (28.4)		-	-	-
Breastfeeding in the first hour of life	No	-	-	-	52	17 (32.7)	0.51	-	-	-
	Yes	-	-	-	162	46 (28.4)		-	-	-
Breastfeeding duration	<6 months	-	-	-	16	7 (43.8)	0.01	-	-	-
	6-11 months	-	-	-	99	36 (36.4)		-	-	-
	≥12 months	-	-	-	102	20 19.6)		-	-	-
Antibiotics in the first year of life	No	-	-	-	55	9 (16.4)	0.02	-	-	-
	Yes	-	-	-	162	54 (33.3)		-	-	-

LRTI in the first year of life	No	-	-	-	102	25 (24.5)	0.17	-	-	-
	Yes	-	-	-	115	38 (33.0)		-	-	-
Number of siblings	0	57	17 (29.8)	0.13	44	13 (29.6)	0.44	13	4 (30.8)	0.17
	1	145	33 (22.8)		103	26 (25.2)		42	7 (16.7)	
	≥2	118	40 (33.9)		70	24 (34.3)		48	16 (33.3)	
Number of people living in the same house	<4	70	22 (31.4)	0.49	49	18 (36.7)	0.18	21	4 (19.1)	0.58
	≥4	250	68 (27.2)		168	45 (26.8)		82	23 (28.1)	
Co-sleeping with parents	No	90	26 (28.9)	0.85	44	13 (29.5)	0.93	46	13 (28.3)	0.67
	Yes	230	64 (27.8)		173	50 (28.9)		57	14 (24.6)	
Daycare center	No	47	12 (25.5)	0.67	23	5 (21.7)	0.42	24	7 (29.2)	0.71
	Yes	273	78 (28.6)		194	58 (29.9)		79	20 (25.3)	
Dog exposure	No	158	47 (29.8)	0.52	99	36 (36.4)	0.03	59	11 (18.6)	0.04
	Yes	162	43 (26.5)		118	27 (22.9)		44	16 (36.4)	
Cat exposure	No	188	46 (24.5)	0.08	126	33 (26.2)	0.28	62	13 (21.0)	0.14
	Yes	132	44 (33.3)		91	30 (33.0)		41	14 (34.1)	
Food allergy	No	292	77 (26.4)	0.02	198	54 (27.3)	0.07	94	23 (24.5)	0.24
	Yes	28	13 (46.4)		19	9 (47.4)		9	4 (44.4)	
Diagnosed asthma	No	276	73 (26.4)	0.10	184	49 (26.6)	0.07	92	24 (26.1)	0.59
	Yes	44	17 (38.6)		33	14 (42.4)		11	3 (27.3)	
Diagnosed eczema	No	247	57 (23.1)	<0.01	166	41 (24.7)	0.01	81	16 (19.8)	<0.01
	Yes	73	33 (45.2)		51	22 (43.1)		22	11 (0.50)	
Current house innovation	No	295	80 (27.1)	0.17	200	57 (28.5)	0.56	95	23 (24.2)	0.20
	Yes	25	10 (40.0)		17	6 (35.3)		8	4 (0.50)	

Abbreviation: VD, vaginal delivery; CS, cesarean section; MS, maternal smoking; LRTI, low respiratory tract infection

Table 3. Factors related to allergic rhinitis

Factors		**All (n =320)**			**6-7 years (n =217)**			**13-14 years (n=103)**		
		N	**n (%)**	**P**	**N**	**n (%)**	**P**	**N**	**n (%)**	**P**
Age (year)	6-7	217	63 (29.0)	0.60	-	-	-	-	-	-
	13-14	103	27 (26.2)		-	-	-	-	-	-
Sex	Male	157	43 (28.8)	0.77	99	31 (31.3)	0.50	58	12 (20.7)	0.15
	Female	163	47 (27.4)		118	32 (27.1)		45	15 (33.3)	
Parental allergy	No	265	64 (24.2)	<0.01	180	44 (24.4)	<0.01	85	20 (23.5)	0.18
	Yes	55	26 (47.3)		37	19 (51.4)		18	7 (38.9)	
Living place	Rural	208	59 (28.4)	0.90	147	44 (29.9)	0.67	61	15 (24.6)	0.65

	Urban	112	31 (27.7)		70	19 (27.1)		42	12 (28.6)	
Truck traffic	Never	12	3 (25,0)	0.97	9	2 (22.2)	0.90	3	1 (50.0)	0.85
	Sometime	173	49 (28.3)		119	36 (30.3)		54	13 (24.1)	
	Always	135	38 (28.1)		89	25 (28.1)		46	13 (28.3)	
Birth delivery	VD	228	62 (27.2)	0.56	151	42 (27.8)	0.55	77	20 (26.0)	0.92
	CS	92	28 (30.4)		66	21 (31.8)		26	7 (26.9)	
Gestational age	≤24	115	25 (21.7)	0.11	77	14 (18.2)	0.01	38	11 (28.9)	0.71
	24-35	194	63 (32.5)		135	49 (36.3)		59	14 (23.7)	
	≥ 35	11	2 (18.2)		5	0 (0.0)		6	2 (33.3)	
Smoking during pregnancy	No	-	-	-	102	25 (24.5)	0.27	-	-	-
	Passive MS	-	-	-	113	37 (32.7)		-	-	-
	Active MS	-	-	-	2	1 (50.0)		-	-	-
Birthweight	≤2500 g	-	-	-	27	9 (33.3)	0.60	-	-	-
	>2500 g	-	-	-	190	54 (28.4)		-	-	-
Breastfeeding in the first hour of life	No	-	-	-	52	17 (32.7)	0.51	-	-	-
	Yes	-	-	-	162	46 (28.4)		-	-	-
Breastfeeding duration	<6 months	-	-	-	16	7 (43.8)	0.01	-	-	-
	6-11 months	-	-	-	99	36 (36.4)		-	-	-
	≥12 months	-	-	-	102	20 19.6)		-	-	-
Antibiotics in the first year of life	No	-	-	-	55	9 (16.4)	0.02	-	-	-
	Yes	-	-	-	162	54 (33.3)		-	-	-
LRTI in the first year of life	No	-	-	-	102	25 (24.5)	0.17	-	-	-
	Yes	-	-	-	115	38 (33.0)		-	-	-
Number of siblings	0	57	17 (29.8)	0.13	44	13 (29.6)	0.44	13	4 (30.8)	0.17
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Diagnosed eczema	No	247	57 (23.1)	<0.01	166	41 (24.7)	0.01	81	16 (19.8)	<0.01
	Yes	73	33 (45.2)		51	22 (43.1)		22	11 (0.50)	
Current house innovation	No	295	80 (27.1)	0.17	200	57 (28.5)	0.56	95	23 (24.2)	0.20
	Yes	25	10 (40.0)		17	6 (35.3)		8	4 (0.50)	

Abbreviation: LRTI, low respiratory tract infection

* Multivariable logistic regression mode for interactive variables (p<0.1 in univariable logistic regression)

⁑ The data is limited to a group of 6-7 years to minimize recall bias

4. DISCUSSION

The findings from our study revealed that the prevalence of current allergic rhinitis (AR) in children aged 6-7 years was 29.0%. This is slightly higher than the 27.6% reported in the ISAAC study conducted in the Hanoi area [3], but the difference was not statistically significant. The prevalence of the 13-14-year age group in our study was 26.2%. The average global prevalence of current AR for these age groups was 9.1% and 16%, respectively, with the Asia-Pacific region at 5.8% and the ISAAC phase III study at 14.5% [7]. Our findings indicate a higher prevalence in both age groups. Additionally, our study confirms that parental atopy is a risk factor for the development of AR, which aligns with the results of other studies [3, 7]. Both genetic and environmental factors are

important in the etiology of AR, suggesting a complex interaction between these factors [5].

The results emphasized the link between parental allergies and the likelihood of children developing AR. Children with a parental history of allergies were 2.39 times more likely to have AR than those without such a history (OR=2.39; 95%CI: 1.24–4.61), p<0.05). The results of our study are also consistent with the previous report, which concluded that a genetic background in terms of a family history of allergic disease is the most potent risk factor for the development of allergic diseases and allergic symptoms [5].

Our research also indicated that children with eczema and skin allergies are significantly associated with an increased risk of developing allergic rhinitis (AR) (p<0.05). Specifically, children with eczema and skin allergies were 1.92 times more likely to develop AR than those without these conditions (OR=1.92; 95% CI: 1.04-3.56; p=0.04). This risk was even higher in the 13-14 year age group, which was 4.26 times greater (OR=4.26; 95% CI: 1.44-12.6; p<0.01). These findings are consistent with the study by von Kobyletzki et al., which showed that children with eczema at baseline were three times more likely to develop AR than those without atopic eczema, highlighting eczema as one of the most substantial risk factors for AR. Early identification of eczema can be valuable in predicting the progression of allergic conditions [8].

The WHO recommends prolonged breastfeeding for six months or more [9]. Our study found a significant association between breastfeeding duration and AR risk (p<0.05). Specifically, children who were breastfed for more than 12 months had a 0.23 times lower risk of developing AR than those who were breastfed for less than six months (OR=0.23; 95% CI: 0.06-0.85). Similarly, research by Han et al. demonstrated that long-term breastfeeding (>12 months) was significantly associated with a reduced incidence of AR compared to short-term breastfeeding (<6 months) [10]. Theories suggest that the interaction between immune antibodies in breast milk and the immune system of infants may play a role, with studies showing that airborne allergens inhaled by breastfeeding infants can stimulate the production of regulatory T cells (Tregs) and promote allergen-specific tolerance [11].

Additionally, our analysis showed that the use of antibiotics during the first year of life is significantly associated with an increased risk of allergic rhinitis (AR) (p=0.02). Children who were given antibiotics in their first year had a 2.56 times higher risk of developing AR compared to those who did not use antibiotics (OR=2.56; 95% CI=0.17-6.61). Ni et al. reported that lifetime antibiotic exposure is significantly associated with AR [12]. Furthermore, their study suggested that early exposure to antibiotics may lead to intestinal dysbiosis, which can disrupt the regulation of the immune system in young children, potentially contributing to the development of chronic respiratory and allergic conditions such as asthma and hay fever. However, when we analyzed the data using a multiple regression model, we found no significant association between antibiotic use in the first years of life and AR.

The analysis also revealed that exposure to dogs was linked to a reduced risk of allergic rhinitis (AR) in children aged 6-7 years (p<0.05). This finding supports current evidence suggesting that dog exposure is a protective factor against the development of AR [13]. A strong association was also found between food allergies and AR (p = 0.02). Children with food allergies were 1.56 times more likely to develop AR compared to those without food allergies (OR=1.56; 95% CI=0.65-3.74). This relationship can be explained by the role of immunoglobulin E (IgE) in allergies. Young children with food sensitivities or confirmed IgE-mediated food allergies are more prone to developing AR and asthma compared to their non-allergic peers [14]. However, we found no significant association between a personal history of food allergies and AR when we conducted a multiple regression analysis.

Our study also identified gestational age as a factor related to allergic rhinitis (AR). Children born to mothers aged between 24 and 35 years had a 1.86 and 2.53 times higher risk of developing AR compared to those born to mothers aged 24 years or younger, both in the overall group of children (OR=1.86; 95% CI=1.05-3.28; p=0.03) and specifically in children aged 6-7 years (OR=2.53; 95% CI=1.19-2.39; p=0.02). Lu et al. also found that a higher maternal age at birth (≥40 years) was associated with 5.24 times increased incidence of AR compared to maternal ages between 25-39 years, with each 5-year increase in maternal age linked to an 18% increase in the rate of physician-diagnosed AR (OR=1.18; 95% CI=1.01-1.39; p=0.045) [15]. The mechanisms by which maternal age at birth influences the development of AR in children are not fully understood. However, one study found that maternal age positively correlated with higher

total serum IgE concentrations in children, a known predictor of later allergic sensitization [16].

Our study has several limitations. First, the sample size is smaller than other studies, which may affect the generalizability of the findings. Second, while useful as an epidemiological tool for screening allergic conditions, the ISAAC questionnaire does not provide a definitive diagnosis. Clinical examinations and specific IgE tests are necessary to confirm the presence of AR. Third, recall bias could have influenced the results, as participants may not accurately remember or report past events. To better assess the development of AR over time, a more rigorous study design incorporating a longitudinal approach should be considered.

5. CONCLUSION

Certain environmental and genetic factors were associated with AR in children aged 6-7 and 13-14 within a small contemporary pediatric outpatient cohort. However, a large-scale study is needed to validate these findings.

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