# Association between allergic rhinitis and despair, suicidal ideation, and suicide attempts in Korean adolescents: a nationally representative study of one million adolescents

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**Abstract.** – OBJECTIVE: There is a lack of studies establishing the association between allergic rhinitis (AR) and despair, suicidal thinking, and suicide attempts in adolescents and children at a population level. This study aimed to investigate whether there are associations between allergic rhinitis and despair, suicidal thinking, and suicide attempts.

**PATIENTS AND METHODS:** The study utilized data from middle through high school adolescents from 2005-2021 who enrolled in the Korea Youth Risk Behavior Web-based Survey (KYRBS; 1,067,169). We assessed despair, suicidal thinking, and suicide attempts in the context of both non-atopic and atopic AR. Multivariable analysis was used to determine the association of variables.

**RESULTS:** The prevalence of allergic rhinitis was 28.0%. 1,067,169 enrolled participants were included in the final analysis. There were 299,468 individuals with allergic rhinitis and 767,701 without. In the context of AR, adolescents were more likely to have despair [adjusted odds ratio (aOR), 1.16; 95% CI, 1.15-1.17], suicidal thoughts (aOR, 1.12; 95% CI, 1.11-1.13 for model 2), and suicide attempts (aOR, 1.13; 95% CI, 1.10-1.15 for model 2). Individuals with atopic AR were more likely in almost all measures to have despair, suicidal thinking, and suicide attempts than individuals with non-atopic AR. Females with AR were more likely to have suicide attempts and middle school students were more likely to have despair, suicidal thoughts, and suicide attempts.

**CONCLUSIONS:** The results of this study warrant future studies investigating why AR is so closely associated with despair, suicidal ideation, and suicide attempts, with the goal of establishing suicide prevention strategies as well as improving overall mental health for adolescents.

Key Words:

Allergic rhinitis, Despair, Suicidal ideation, Suicide attempts.

# Introduction

Allergic Rhinitis (AR), which can also be called allergic rhinoconjunctivitis when the eyes are involved, is an inflammatory condition characterized by at least one of the following: nasal congestion, rhinorrhea, itching, and sneezing<sup>1,2</sup>. It is triggered by specific immunoglobulin E (sIgE) to aeroallergens in the environment and can be "mixed" rhinitis as well, meaning it is also exacerbated by irritants, such as extremely cold weather, not just allergens. Symptomatic AR usually begins by 7 years of age<sup>3</sup> and naturally progresses to become more persistent and worsen throughout childhood<sup>4,5</sup>.

AR is a significant burden to the population, affecting over 400 million individuals worldwide<sup>6</sup> with a prevalence of around 14% of the global population<sup>7</sup>. It also significantly affects the quality of life of many patients. The measures that have been seen to be affected include



impairment of physical and social functioning, disturbed sleep, daytime somnolence and fatigue, irritability, depression, and attention, learning and memory deficit<sup>3</sup>. Numerous studies<sup>8</sup> have found that allergies are associated with increased depressive symptoms, including suicidal thoughts/attempts. This indicates that atopic disorders such as allergic rhinitis significantly affect not just patients' physical health but also their mental health.

While this relationship has been clearly observed, there are not many studies on a large population scale determining an association between despair, suicidal thinking, and suicide attempts, and allergic rhinitis in adolescents in rapidly developed countries. Especially in adolescence, patients are already vulnerable due to increased psychological burden, which leads to increased suicidal ideation and attempts<sup>8,9</sup>. In the context of continually rising rates of suicide in adolescents due to the mounting pressures of school and peer issues, increasing AR burden will likely exacerbate such vulnerability. Therefore, to better understand this issue, we aimed to establish whether despair, suicidal thinking, and suicide attempts are associated with the presence of allergic rhinitis in adolescents.

# **Patients and Methods**

# Study Subjects

This study involved a secondary analysis of data obtained from the Korea Youth Risk Behavior Web-based Surveys (KYRBS) conducted between 2005 and 2021. The KYRBS is an annual survey conducted by the Korea Disease Control and Prevention Agency (KDCA) to assess health-risk behaviors among Korean children and adolescents aged 13 to 18 years<sup>10-12</sup>. The survey consists of 15 sections, covering various topics such as socioeconomic status, diet, physical activity, obesity, mental health, and substance use.

The KYRBS uses a three-stage random cluster sampling method to obtain a nationally representative sample of students. Approximately 75,000 students from 400 middle schools and 400 high schools are selected each year using proportional sampling based on the target population composition. Sample schools are then chosen using systematic sampling, and sample classes are selected using simple random sampling. The survey is conducted in June and July each year, and students complete the survey anonymously by logging on to survey internet webpages with an assigned unique identification number. Parental permission is obtained before the survey, and students with special educational needs are excluded from participation. The data for this study included responses from 1,067,169 participants across 16 years of surveys. The KYRBS data were anonymized, and the study was approved by the Institutional Review Board of the KDCA and Kyung Hee University (KHUH 2022-06-042).

Written informed consent was obtained from the participants or their parents involved in this study.

# Exposure and Endpoint

Cases of AR were included on the basis of having been diagnosed by a physician within the past 12 months<sup>2</sup>. Atopic AR was considered as AR with at least one additional allergic disease (asthma and atopic dermatitis)<sup>13</sup>. Adolescents were surveyed about their experiences with despair that affected their social lives for a duration of two weeks (referred to as 'despair'), thoughts of suicide ('thinking of suicide'), and any suicide attempts within the past year ('suicide attempt')<sup>14</sup>.

#### Statistical Analysis

The study used data from the KYRBS, which was collected through a representative, stratified, and clustered sampling process. Descriptive statistics were conducted to analyze the clinical characteristics of the study population, and numbers and percentages were used for each variable. Chi-squared tests were performed for categorical variables, and independent Student *t*-tests were performed for continuous variables to compare adolescents with and without  $AR^{15}$ . In particular, Chi-squared tests were used to determine the statistical significance of changing trends in despair and suicidal thoughts in adolescents with AR. Multivariable logistic regression analysis was utilized to determine the associated factors for despair, suicidal thoughts, and suicide attempts in adolescents with AR16. Odds ratios (ORs), adjusted ORs (aORs), and 95% confidence intervals (95% CIs) were obtained through three models: (i) simple logistic regression with complex sampling (unadjusted), (ii) multivariable logistic regression with complex sampling after adjustment for sex and age (model 1), and (iii) multivariable logistic regression with complex sampling after adjustment for sex, age, body mass index (BMI) group, smoking status, alcohol consumption, parents' highest educational level, school performance, and subjective stress.

SAS software, version 9.3 (SAS Institute Inc, Cary, NC, USA), was used for all statistical analyses, and all statistical tests were 2-sided, with a *p*-value lower than .05 indicating statistical significance.

# Results

# Demographic Characteristics

Table I contains the clinical characteristics of the adolescents in this study. There was a total of 1,067,169 subjects: 767,701 without allergic rhinitis and 299,468 with allergic rhinitis. The mean age was 15.41 years, with 51.44% of participants being males and 48.56% being females (Table I).

# Associations of Allergic Rhinitis and Despair, Suicidal Thinking, and Suicide Attempts in Study Subjects

Multivariable logistic regression analysis showed that adolescents with allergic rhinitis were more likely to have despair (OR, 1.12; 95% CI, 1.10-1.13 for crude OR; aOR, 1.10; 95% CI, 1.09-1.11 for model 1; aOR, 1.16; 95% CI, 1.15-1.17 for model 2) and suicidal thoughts (OR, 1.06; 95% CI, 1.05-1.07 for crude OR; aOR, 1.06; 95% CI, 1.05-1.07 for model 1; aOR, 1.12; 95% CI, 1.11-1.13 for model 2). For suicide attempts, the crude OR showed no significant difference (OR, 1.02; 95% CI, 0.99-1.04) but did show increased likelihood with both model 1 and 2 aOR (aOR, 1.03; 95% CI, 1.01-1.06 for model 1; aOR, 1.13; 95% CI, 1.10-1.15 for model 2) (Table II).

Adolescents with non-atopic AR (AR without atopic dermatitis and asthma) were more likely to have despair (OR, 1.05; 95% CI, 1.03-1.06 for crude OR; aOR, 1.03; 95% CI, 1.02-1.05 for model 1; and aOR, 1.09; 95% CI, 1.08-1.10 for model 2); however, they were only found to have increased suicidal thoughts with model 2 adjusted OR (aOR, 1.04; 95% CI, 1.03-1.06) with a decreased likelihood on crude OR (OR, 0.98; 95% CI, 0.97-0.99) and no significant difference on model 1 adjusted OR (aOR 0.99; 95% CI, 0.97-1.00). For suicide attempts, both crude OR and model 1 adjusted OR showed decreased likelihood (OR, 0.90; 95% CI, 0.88-0.93 for crude OR; aOR, 0.93; 95% CI, 0.90-0.96 for model 1) while model 2 adjusted OR showed no significance (OR, 1.014; 95% CI, 0.98-1.05) (Table II).

Multivariable logistic regression analysis showed that adolescents with atopic AR (AR with concomitant atopic dermatitis and asthma) were more likely to have despair (OR, 1.22; 95% CI, 1.21-1.24 for crude OR; aOR, 1.19; 95% CI, 1.18-1.21 for model 1; aOR, 1.26; 95% CI, 1.24-1.27 for model 2), suicidal thoughts (OR, 1.188; 95% CI, 1.17-1.21 for crude OR; aOR, 1.17; 95% CI, 1.15-1.19 for model 1; aOR, 1.26; 95% CI 1.22-1.26 for model 2), and suicide attempts (OR, 1.19; 95% CI, 1.15-1.22 for crude OR; aOR, 1.19; 95% CI, 1.15-1.22 for model 1; aOR, 1.28; 95% CI, 1.24-1.33 for model 2), respectively (Table II).

# *Stratified Analysis of the Associations of Allergic Rhinitis and Despair, Suicidal Thinking, and Suicide Attempt in Study Subjects*

In Table III, the results of the stratified multivariable analyses for individuals with AR showed that females with allergic rhinitis were more likely to have suicide attempts [aOR (95% CI); 1.20 (0.98-1.16-1.23) vs. 1.01 (0.98-1.06)]. It also found that middle school students with AR were more likely than high school students to have despair [aOR (95% CI); 1.17 (1.15-1.19) vs. 1.04 (1.03-1.06)], suicidal thoughts [aOR (95% CI); 1.15 (1.13-1.17) vs. 1.08 (1.07-1.10)], and suicide attempts [aOR (95% CI); 1.18 (1.15-1.22) vs. 1.105 (1.01-1.09)]. The results also showed that those in the high economic status were more likely to have AR than those in the low economic status with crude OR [OR (95% CI); 1.17 (1.14-1.21) vs. 1.12 (1.10-1.13)].

# Discussion

This population-based cross-sectional study in adolescents suggests that adolescents with allergic rhinitis have a higher chance of having despair, suicidal thoughts, and suicidal ideation. We also found that patients with AR who also had atopic dermatitis and asthma were more likely than patients with just allergic rhinitis to have despair, suicidal thoughts, and suicidal ideation. Females were found to have more suicide attempts, and middle school students were more likely to have all three measures than high school students. This study is one of the first to find adolescents in middle school as more at risk of suicide than those in high school as well as to investigate the difference between non-atopic and atopic AR.

The results we obtained suggest that allergic rhinitis is independently associated with an increased risk of suicide-related behaviors in adolescents, which was more prominent in patients with a more atopic picture of allergic rhinitis as

	Total	Subjects with AR	Subjects without AR	
Number, n	1,067,169	299,468	767,701	
Age, mean (SD)	15.41 (1.69)	15.55 (1.69)	15.35 (1.69)	
Sex, % (95% CI)		()		
Female	48.56 (48.47 to 48.66)	48.98 (48.80 to 49.16)	48.40 (48.28 to 48.51)	
Male	51.44 (51.35 to 51.53)	51.02 (50.84 to 51.20)	51.60 (51.49 to 51.72)	
Region	51.11 (51.55 to 51.55)	51.02 (50.01 to 51.20)	51.00 (51.15 to 51.72)	
Urban	46.44 (46.35 to 46.54)	47.16 (46.98 to 47.34)	46.17 (46.05 to 46.28)	
Rural	53.56 (53.46 to 53.65)	52.84 (52.66 to 53.02)	53.84 (53.72 to 53.95)	
Body mass index group, % (95% CI)*	55.56 (55.16 to 55.65)	52.01 (52.00 to 55.02)	55.61 (55.72 to 55.55)	
Underweight	24.91 (24.83 to 24.99)	23.28 (23.13 to 23.43)	25.55 (25.45 to 25.64)	
Normal	53.02 (52.92 to 53.11)	53.34 (53.16 to 53.52)	52.89 (52.78 to 53.00)	
Overweight	11.27 (11.21 to 11.33)	11.81 (11.69 to 11.92)	11.06 (10.99 to 11.13)	
Obese	10.80 (10.74 to 10.86)	11.58 (11.46 to 11.69)	10.50 (10.43 to 10.57)	
Smoking status, % (95% CI)	10.80 (10.74 to 10.80)	11.38 (11.40 to 11.09)	10.50 (10.45 to 10.57)	
Non-smoker	79.70 (79.62 to 79.77)	81.67 (81.54 to 81.81)	78.92 (78.83 to 79.01)	
Smoker	20.30 (20.23 to 20.38)			
Alcohol consumption, % (95% CI)	20.30 (20.23 to 20.38)	18.33 (18.19 to 18.46)	21.08 (20.99 to 21.17)	
Non-drinker	81.43 (81.35 to 81.50)	$92.66(92.52 \pm 2.92.90)$	90.04 ( $90.95$ to $91.02$ )	
		82.66 (82.53 to 82.80)	80.94 (80.85 to 81.03)	
1-2 day	10.81 (10.75 to 10.86)	10.35 (10.24 to 10.46)	10.98 (10.91 to 11.05)	
3-5 day	3.40 (3.37 to 3.44)	3.22 (3.16 to 3.28)	3.48 (3.43 to 3.52)	
6-9 day	2.04 (2.02 to 2.07)	1.77 (1.72 to 1.82)	2.15 (2.12 to 2.18)	
$\geq$ 10 day	2.32 (2.30 to 2.35)	2.00 (1.95 to 2.05)	2.45 (2.42 to 2.49)	
Educational level, % (95% CI)	50,00 (50,00 (	40.70 (40.54 ( 40.00)	52 (0 (52 50 ) 52 00)	
Middle school	52.29 (52.20 to 52.39)	48.72 (48.54 to 48.89)	53.69 (53.58 to 53.80)	
High school	47.71 (47.61 to 47.80)	51.28 (51.11 to 51.46)	46.31 (46.20 to 46.42)	
Parents' highest educational level, % (95% CI)	45 40 (45 20 ) 45 50			
University graduated or higher	45.49 (45.39 to 45.58)	53.61 (53.43 to 53.79)	42.32 (42.21 to 42.43)	
High school graduated	26.56 (26.47 to 26.64)	22.68 (22.53 to 22.83)	28.07 (27.97 to 28.17)	
Middle school graduated or under	1.804 (1.779 to 1.829)	0.998 (0.962 to 1.033)	2.118 (2.086 to 2.151)	
Unknown	26.15 (26.07 to 26.24)	22.71 (22.56 to 22.86)	27.50 (27.40 to 27.60)	
Economic level, % (95% CI)				
Low	15.30 (15.23 to 15.37)	14.68 (14.55 to 14.81)	15.54 (15.46 to 15.62)	
Middle	49.08 (48.99 to 49.18)	48.00 (47.82 to 48.18)	49.50 (49.39 to 49.61)	
Upper-middle	27.39 (27.30 to 27.47)	28.71 (28.55 to 28.87)	26.87 (26.77 to 26.97)	
High	8.235 (8.182 to 8.287)	8.613 (8.512 to 8.713)	8.087 (8.026 to 8.148)	
School performance, % (95% CI)				
Low	9.34 (9.28 to 9.39)	8.21 (8.11 to 8.31)	9.78 (9.71 to 9.84)	
Lower-middle	23.25 (23.17 to 23.33)	21.55 (21.41 to 21.70)	23.91 (23.81 to 24.00)	
middle	29.07 (28.99 to 29.16)	27.99 (27.83 to 28.15)	29.50 (29.40 to 29.60)	
Upper-middle	25.90 (25.82 to 25.99)	27.77 (27.61 to 27.93)	25.18 (25.08 to 25.27)	
High	12.44 (12.38 to 12.50)	14.48 (14.35 to 14.60)	11.64 (11.57 to 11.72)	
Asthma, % (95% CI)	7.232 (7.183 to 7.281)	14.65 (14.53 to 14.78)	4.34 (4.29 to 4.38)	
Atopic dermatitis, % (95% CI)	19.78 (19.71 to 19.86)	31.96 (31.79 to 32.12)	15.03 (14.95 to 15.11)	
Stress, % (95% CI)				
Mild	17.78 (17.71 to 17.85)	15.75 (15.62 to 15.88)	18.57 (18.49 to 18.66)	
Moderate	42.14 (42.05 to 42.23)	41.36 (41.19 to 41.54)	42.44 (42.33 to 42.55)	
High	29.28 (29.19 to 29.37)	30.97 (30.80 to 31.13)	28.62 (28.52 to 28.72)	
Severe	10.80 (10.74 to 10.86)	11.92 (11.80 to 12.04)	10.36 (10.29 to 10.43)	
Despair in the past year, % (95% CI)	30.60 (30.51 to 30.69)	32.27 (32.10 to 32.44)	29.95 (29.84 to 30.05)	
Suicidal thoughts in the past year, % (95% CI)	15.85 (15.78 to 15.92)	16.43 (16.30 to 16.56)	15.63 (15.55 to 15.71)	
Suicide attempt in the past year, % (95% CI)	3.414 (3.380 to 3.449)	3.453 (3.388 to 3.519)	3.399 (3.358 to 3.440)	
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#### Table I. Demographic characteristics of Korean adolescents from KYRBS, 2005 to 2021.

BMI, body mass index; CI, confidence interval; SD, standard deviation. \*The body mass index (BMI) was classified into four categories in accordance with the 2017 Korean National Growth Charts: underweight (less than 5<sup>th</sup> percentile), normal (between 5<sup>th</sup> and 84<sup>th</sup> percentile), overweight (between 85<sup>th</sup> and 94<sup>th</sup> percentile), and obese (above 95<sup>th</sup> percentile).

well as middle school adolescents and females. There have been studies<sup>17-20</sup> in the past that have demonstrated a similar connection between AR

and anxiety, depression and suicidal behaviors. These results are also consistent with studies<sup>21,22</sup> that found that adolescents aged 12-14 years are Table II. Multivariable analysis of the associations of despair, suicidal thoughts, and suicide attempts with allergic rhinitis among Korean adolescents (total n = 1,067,169).

		Independent variable							
_	Despair			Suicidal thoughts		Suicide attempts			
 Dependent variable	Crude OR (95% CI)	Adjusted OR (95% Cl; model 1)	Adjusted OR (95% Cl; model 2)	Crude OR (95% Cl)	Adjusted OR (95% Cl; model 1)	Adjusted OR (95% Cl; model 2)	Crude OR (95% CI)	Adjusted OR (95% Cl; model 1)	Adjusted OR (95% CI; model 2)
Overall									
Without AR	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
With AR	1.115 (1.104 to 1.125)	1.096 (1.176 to 1.207)	1.157 (1.147 to 1.168)	1.062 (1.049 to 1.074)	1.062 (1.050 to 1.074)	1.121 (1.108 to 1.134)	1.017 (1.993 to to 1.040)	1.034 (1.010 to 1.058)	1.125 (1.099 to 1.152)
By atopic status									
Without AR	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
With atopic AR	1.222 (1.206 to 1.238)	1.192 (1.176 to 1.207)	1.258 (1.241 to 1.274)	1.188 (1.169 to 1.207)	1.173 (1.154 to 1.192)	1.235 (1.215 to 1.255)	1.186 (1.150 to 1.224)	1.186 (1.149 to 1.224)	1.283 (1.243 to 1.325)
With non- atopic AR	1.045 (1.034 to 1.057)	1.034 (1.023 to 1.046)	1.092 (1.079 to 1.104)	0.979 (0.965 to 0.993)	0.988 (0.974 to 1.002)	1.044 (1.029 to 1.059)	0.903 (0.876 to 0.930)	0.928 (0.901 to 0.956)	1.014 (0.984 to 1.045)

AR, allergic rhinitis; CI, confidence interval; OR, odds ratio. Adjusted model 1: adjusted for sex and age. Adjusted model 2: adjusted for sex, age, body mass index group (underweight, normal, overweight, and obese), smoking status, alcohol consumption, parents' highest educational level (high, middle-high, middle-low, and low), school performance (high, middle-high, middle, middle-low, and low), school performance (high, middle-high, middle, middle-low, and low), school performance (high, middle, middle-high, middle). Numbers in bold correspond to significant differences (p < 0.05).

Table III. Stratified analysis of the associations of despair, suicidal thoughts, and suicide attempts with allergic rhinitis	mong Korean adolescents (total $n = 1,067,169$ ).	
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		Independent variable							
_	Despair			Suicidal thoughts		Suicide attempts			
 Dependent variable	Crude OR (95% CI)	Adjusted OR (95% CI; model 1)	Adjusted OR (95% CI; model 2)	Crude OR (95% Cl)	Adjusted OR (95% CI; model 1)	Adjusted OR (95% CI; model 2)	Crude OR (95% CI)	Adjusted OR (95% CI; model 1)	Adjusted OR (95% Cl; model 2)
Male Female School	1.10 (1.08 to 1.11) 1.13 (1.11 to 1.14)	1.08 (1.07 to 1.10) 1.11 (1.10 to 1.12)	1.12 (1.11 to 1.14) 1.17 (1.15 to 1.18)	1.06 (1.04 to 1.08) 1.06 (1.04 to 1.08)	1.06 (1.04 to 1.08) 1.07 (1.05 to 1.08)	1.10 (1.08 to 1.12) 1.13 (1.11 to 1.15)	0.94 (0.91 to 0.98) 1.06 (1.03 to 1.09)	0.95 (0.91 to 0.98) 1.09 (1.06 to 1.12)	1.01 (0.98 to 1.06) 1.20 (1.16 to 1.23)
Middle school High school Economic level	1.11 (1.09 to 1.12) 1.10 (1.08 to 1.11)	1.11 (1.09 to 1.12) 1.09 (1.07 to 1.10)	1.17 (1.15 to 1.19) 1.13 (1.12 to 1.15)	1.09 (1.07 to 1.10) 1.04 (1.03 to 1.06)	1.09 (1.07 to 1.11) 1.04 (1.02 to 1.06)	1.15 (1.13 to 1.17) 1.08 (1.07 to 1.10)	1.08 (1.05 to 1.11) 0.97 (0.94 to 1.00)	1.09 (1.05 to 1.12) 0.97 (0.94 to 1.01)	1.18 (1.15 to 1.22) 1.05 (1.01 to 1.09)
Low (low and low-middle)	1.12 (1.10 to 1.13)	1.10 (1.09 to 1.12)	1.14 (1.13 to 1.16)	1.07 (1.05 to 1.08)	1.07 (1.05 to 1.09)	1.12 (1.10 to 1.14)	1.04 (1.01 to 1.08)	1.06 (1.03 to 1.10)	
High (high- middle and high)	1.17 (1.14 to 1.21)	1.14 (1.10 to 1.18)	1.18 (1.14 to 1.22)	1.11 (1.07 to 1.16)	1.10 (1.05 to 1.14)	1.14 (1.09 to 1.18)	1.00 (0.93 to 1.08)	1.00 (0.93 to 1.08)	1.08 (1.00 to 1.17)

AR, allergic rhinitis; CI, confidence interval; OR, odds ratio. Adjusted model 1: adjusted for sex and age.

at a higher risk of fatal self-harm than those aged 15-17 years and that females have a higher suicidal rate in adolescence. In addition, a cross-sectional study<sup>23</sup> using a nationwide population-based prospective cohort found an association between AR in early adolescence and depression in late adolescence and early adulthood. A recent study<sup>24</sup> collecting population-based survey data from 2007-2017 in Korea found similar findings to our own. They determined that female individuals in the context of AR had an increased likelihood of depression, suicidal ideation and suicide attempts. The presence of AR by itself was associated with depression and suicidality, and suicide attempts. While observing a similar population to our own, our study included a larger cohort from 2005-2021 as well as differentiated atopic AR vs. non-atopic AR. We also differentiated between middle school and high school-aged adolescents, finding a significant difference in the context of allergic rhinitis.

There are immunopathogenic mechanisms that may explain our results. In atopic disorders, allergic inflammatory mediators, interleukin (IL)-4, IL-5, and IL-13, are released and perpetuated by "allergic" T helper-2 (TH2) cells<sup>25,26</sup>. Along with atopic dermatitis and asthma, AR is associated with systemic increases of such cytokines<sup>27,28</sup>. A study<sup>29</sup> found an association between inflammatory markers and depression/ suicide attempts, including markers found in allergic diseases. In addition to that, allergy-mediated cytokines can increase arousal, produce aberrations in rapid eye movement (REM) sleep, increase REM latency, and decrease REM duration<sup>30</sup>, thereby reducing sleep quality and, subsequently, quality of life and overall happiness. TH2 sensitization may also lead to deleterious effects on the developing brain, which can ultimately lead to increased attention-deficit/ hyperactivity disorder, depression, anxiety and suicidal ideation<sup>31</sup>. Specifically, early-life overexposure to IL-4, which can occur due to TH2 sensitization from allergic disease, has been reported<sup>32</sup> to reduce myelination and lead to cognitive impairment and developmental delays, and these effects have been found<sup>33</sup> to be inhibited with IL-4 neutralization. These mechanisms of action all point toward a functional correlation between atopy and psychological disorders, including depression. They may also explain the difference between the more allergic picture of AR with concomitant atopic dermatitis and asthma *vs.* just AR alone, in addition to the significant burden AD and asthma independently have on patients.

Looking at the study design, the results are unlikely to be affected by performance bias. Due to the severe nature of suicide-related behaviors, allergic rhinitis is unlikely to result in contrasting detection of suicide-related behaviors between adolescents with and without allergic rhinitis. In addition, our study included subjects for 15 years and yielded the same results every year. We controlled for all potential risk factors of suicide-related behavior to eliminate covariate imbalance. Detection bias is unlikely to explain the association between allergic rhinitis and the risk of suicide-related behaviors since the study subjects took the survey in the same manner.

The strengths of our study include the nationwide survey with a high response rate and adjustment for various confounders, including sex, age, body mass index group, smoking status, alcohol consumption, parent's highest education level, school performance, and subjective assessment of health level. However, our study's limitations are due to its survey-based nature, no data on the incidence of suicide in study subjects, and no inclusion of allergy and/or depression medications. Such medications, including oral corticosteroids and montelukast, may significantly contribute to the outcomes of such a study.

# Conclusions

We found a close relationship between despair, suicidal thinking, and suicide attempts and allergic rhinitis in young adolescents. Not only that, patients with AR with concomitant atopic dermatitis and asthma are at an even higher risk. Future prospective studies are warranted to firmly establish the mechanism of action behind this relationship, corroborate the present findings, and to help implement ways of decreasing suicide-related behaviors in adolescents, especially middle schoolers, with allergic rhinitis in a clinical setting.

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### **Ethics Approval**

The KYRBS data were anonymized, and the study was approved by the Institutional Review Board of the KDCA and Kyung Hee University (KHUH 2022-06-042).

#### **Informed Consent**

Written informed consent was obtained from the participants or their parents involved in this study.

#### Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request (Dong Keon Yon; yonkkang@gmail.com).

#### **Conflicts of Interest**

The authors declare no conflicts of interest.

#### Authors' Contributions

Dr. Dong Keon Yon had full access to all study data and were responsible for ensuring the integrity of the data and the accuracy of the data analysis. All authors approved the final version of the manuscript before submission. Study concept and design: Joong Ki Cho, Hwi Yang, Jaeyu Park, Hojae Lee, Ann Nguyen, Mafaz Kattih, Masoud Rahmati, and Dong Keon Yon; acquisition, analysis, or interpretation of the data: Joong Ki Cho, Hwi Yang, Hojae Lee, Ann Nguyen, Mafaz Kattih, Masoud Rahmati, and Dong Keon Yon; drafting of the manuscript: Joong Ki Cho, Hwi Yang, Hojae Lee, Ann Nguyen, Mafaz Kattih, Masoud Rahmati, and Dong Keon Yon; critical revision of the manuscript for important intellectual content: Joong Ki Cho, Hwi Yang, Hojae Lee, Ann Nguyen, Mafaz Kattih, Masoud Rahmati, and Dong Keon Yon; statistical analysis: Hwi Yang and Hojae Lee; and study supervision: Dong Keon Yon. Hojae Lee, Masoud Rahmati, and Dong Keon Yon contributed equally as corresponding authors. The corresponding authors attest that all listed authors meet the authorship criteria and that no other individuals meeting the criteria have been omitted.

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