ORIGINAL ARTICLE

Dental Caries in Adults with Atopic Dermatitis: A Nationwide Cross-Sectional Study in Korea

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Background: Dental caries is the most prevalent chronic infectious oral disease of multifactorial etiology. Increased risk of dental caries development in patients with asthma and allergic rhinitis has been frequently reported. In contrast, only a few studies on dental caries in patients with atopic dermatitis (AD) have been reported. **Objective:** We investigated the association between AD and dental caries development in an adult population in the Republic of Korea. **Methods:** A total of 21,606 adults who participated in the Korean National Health and Nutrition Examination Survey, a nationwide, population-based, cross-sectional survey between 2010 and 2015, were included in the study. Multiple logistic regression analyses with confounder adjustment suggested odds ratios (ORs) to identify the possible association between AD and decayed, missing, filled teeth (DMFT) experience compared to non-AD participants. Multiple Poisson regression analyses estimated the mean ratio of the DMFT index according to the presence of AD. **Results:** After adjusting for various confounding factors, the prevalence of DMFT was significantly associated with AD (OR, 1.58; 95% confidence interval (CI), $1.08 \sim 2.29$; $p = 0.017$). In addition, the mean value of the DMFT index was significantly different between the AD and non-AD groups (mean ratio, 1.07; 95% CI, $1.00 \sim 1.14$; $p = 0.046$). **Conclusion:** AD was significantly associated with the development of dental caries. Dermatologists should be aware of the dental manifestations of AD patients and recommend regular dental check-ups for the early detection of caries. **(Ann Dermatol 33(2) 154~162, 2021)**

-Keywords-
Adult , Atopic dermatitis, Dental caries

INTRODUCTION

Atopic dermatitis (AD) results from epithelial barrier disturbance and immune dysregulation in the skin of genetically predisposed hosts. Keratinocytes in normal skin produce antimicrobial peptides that are active against pathogens. However, the deficient expression of antimicrobial peptides, including β-defensins and cathelicidins, in AD, may cause microbiota colonization, particularly *Staphylococcus aureus*, which may contribute to either disease onset or aggravation[1,2]. Compared to the $5\% \sim 30\%$ of *S. aureus* skin colonization in healthy individuals, the overexpansion of *S. aureus* appeared in $75\% \sim 100\%$ of AD patients' lesional skin and $30\% \sim 100\%$ of their nonlesional skin[3,4].

Dental caries is one of the most prevalent chronic infectious oral diseases associated with several complications. According to the United States National Health and Nutritional Examination Survey from 2011 to 2016, the prevalence of dental caries in permanent teeth remains high. Approximately 90% of adults aged 20 to 64 years have experienced caries[5]. Its etiology is multifactorial: complex interactions of oral microorganisms in the dental plaque, diet, and host factors, including genetic and immunologic responses[6-8]. Based on the extended ecological hypothesis and environmental acidification, mostly caused by a frequent sugar supply, a microbial shift towards acidogenic (acid-producing) and aciduric (acid-tolerant) populations,

which are cariogenic microflora, occurs[9].

Several previous studies on asthma and allergic rhinitis, which, like AD, are included in atopic diseases, suggested a higher risk of dental caries in the disease group than in the control group[10,11]. However, to the best of our knowledge, only a few studies have assessed the association between dental caries and AD[12,13]. Although the pathogenic mechanisms are not clearly established, it has been hypothesized that there may be a potential link between AD and dental caries. Therefore, this population-based study aimed to determine the association between AD and dental caries in Korean adults with AD.

MATERIALS AND METHODS

Data source

We analyzed data from the Korean National Health and Nutrition Examination Survey (KNHANES), administered by the Korean Centers for Disease Control and Prevention between 2010 and 2015. KNHANES is a continuous annual survey program conducted to involve complex, stratified, multistage, and probability-cluster samples representative of the noninstitutionalized civilian population in the Republic of Korea[14]. This nationwide cross-sectional survey consisted of four components: a health-related interview, a health behavior survey, a health examination, and a nutrition survey.

Study population

From all the data collected from KNHANES, we used the sociodemographic characteristics (age, sex, household income, and insurance type), anthropometric information, oral health-related variables, and survey results regarding AD. AD patients were identified by an affirmative answer to the following question: "Have you ever been diagnosed as atopic dermatitis by a doctor?". We defined the control group as those who answered "No" to the above question. This single question provided sufficient validity for the epidemiological study of AD in an adult population[15].

Sociodemographic and comorbid variables

The sociodemographic data of the participants were obtained through a self-administered questionnaire. These included age, sex, household income, education, and region. Household income was categorized into four groups based on the equalized gross annual household income: <25% (the lowest quartile income group), 25%~50%, 50%~75%, and 75%~100% (the highest income quartile group). Education level was classified as primary school or lower, middle school graduate, high school graduate, and college graduate or higher. Regarding the region of residence, the 16 districts of the Republic of Korea were subdivided into

two groups: (1) urban regions: Seoul, Gyeonggi, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan; and (2) rural regions: Gangwon, Chungbuk, Chungnam, Jeonnam, Jeonbuk, Gyeongbuk, Gyeongnam, and Jeju. We considered household income, education, and region of residence to reflect socioeconomic status. Body mass index (BMI) was calculated as follows: weight (kg)/height^2 (m^2). Information on lifestyle behaviors, including cigarette smoking and alcohol consumption, was also collected. The participants were categorized according to their smoking habits as either smokers, ex-smokers, or nonsmokers. Alcohol intake was classified according to the frequency of consumption as follows: none, occasionally (<2 times/week), and frequently (≥2 times/week). The presence of comorbidities was determined only when the study participants admitted to having been diagnosed with asthma, allergic rhinitis, hypertension, diabetes mellitus, and hyperlipidemia, by a physician.

Oral health examination and survey

To ensure the reliability of oral health examinations, calibration training for the dentists was provided every year by the reference dentist. Caries was assessed based on the experience of decayed, missing, and filled teeth (DMFT) and the total number of DMFT (DMFT index), which is the most common and simplest method of assessing dental caries in oral epidemiology[16]. To assess patients with severe dental caries, the significant caries (SiC) group, which was proposed by the World Health Organization, was also evaluated by identifying the most severely-affected 30% of the participants[17]. Additionally, dental health behaviors, such as the use of auxiliary oral hygiene products (dental floss, interdental brush, and mouthwash), and frequency of daily teeth brushing (per day) were also assessed. Participants were also asked the following question: "Did you have regular dental check-up within one year before the interview?" We considered the term "regular dental checkup" as visits to a dental clinic more than once a year to sustain a healthy oral state, regardless of an apparent dental problem. The self-rated oral health status was a 5-level rating in the questionnaire; we reorganized the subjective oral status into two grades: ratings of poor or very poor being categorized as "poor" and fair to excellent as "healthy".

Frequency of intake of sugar-source foods

Based on the Korea National Health and Nutrition Examination Food Frequency Questionnaire and Preliminary Studies, the intake of three major sugar source foods was surveyed: crackers/cookies, carbonated soft drinks, and ice-cream/sherbet. We divided the patients into three groups based on the frequency of ingestion: almost none, occa-

sionally (<2 times per week), and frequently (≥ 2 times per week).

Ethical considerations

The KNHANES protocol was approved by the Institutional Review Board of the Korean Centers for Disease Control and Prevention (IRB no. 2010-02CON-21-C, 2011-02CON-06-C, 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-03-5C, 2015-01-02-6C), and conducted according to the Declaration of Helsinki. All participants provided written informed consent. This study was approved by the institutional review board (IRB no. ISPAIK 2020-04-021), which waived the requirement for informed consent due to the de-identification of the data obtained from the KNHANES dataset.

Statistical analysis

Statistical analyses were performed with the aid of R ver. 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS ver. 23.0 (IBM Corp., Armonk, NY, USA). To produce unbiased national estimates representing the general Korean population, we used KNHANES sample weights accounting for the complex sampling design of each participant. We calculated the means and standard deviations of the participants' ages. Categorical or ordinal variables were expressed as proportions and standard errors. The differences in participant characteristics according to the presence of these conditions were analyzed using the design-based Wilcoxon rank-sum test for complex sample survey data or the Pearson's χ^2 test with Rao–Scott adjustment. To estimate the odds ratios (ORs) of AD according to the DMFT experience (DMFT index >0), severe dental caries group, and poor subjective oral status, we performed simple and multiple logistic regression analyses using the generalized linear model for a complex survey design. After fulfilling the normality assumption, we conducted simple and multiple Poisson regression analyses, by using the generalized linear model for a complex survey design to compare the DMFT index between the participants with and without AD. In all analyses, two-tailed p-values of <0.05 were considered statistically significant.

RESULTS

Of the 48,482 potentially eligible participants (2008~2014 KNHANES), 26,876 were excluded for the following reasons: age<19 years (n=10,849), incomplete data on AD (n=4,226), non-responders for oral health-related survey or oral examinations (n=1,728), missing values and non-responders with nutritional data (n=9,461), and other incomplete data (n=612). A total of 21,606 participants were included; 21,043 non-AD subjects and 563 subjects with AD (Fig. 1).

The sociodemographic characteristics and comorbidities of the study population are summarized in Table 1. Participants with AD were significantly younger ($p<0.001$), better educated ($p<0.001$), had a higher proportion living in
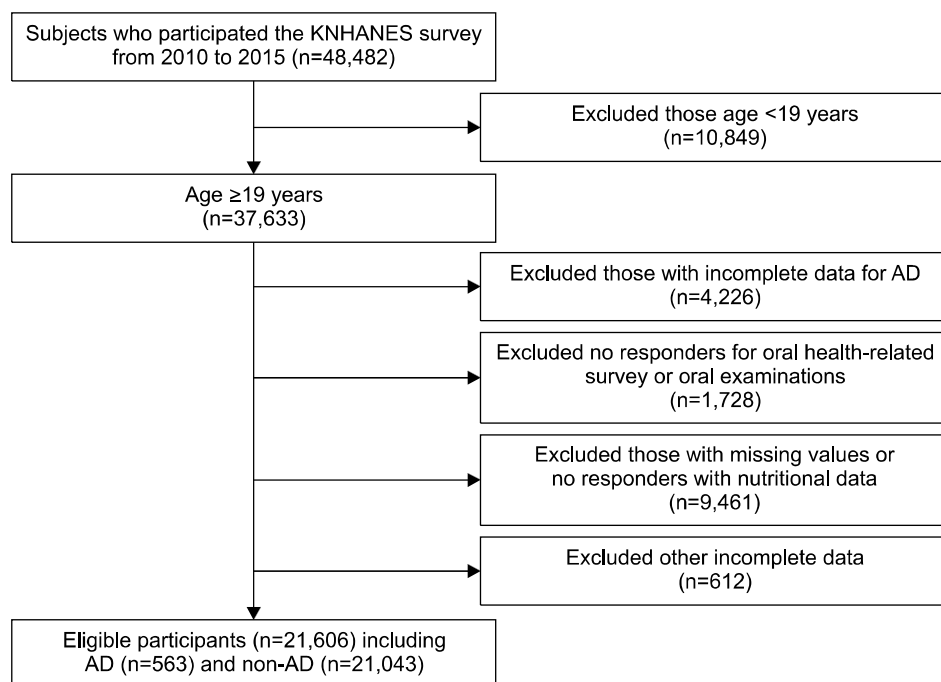

Fig. 1. Flow diagram of the inclusion and exclusion of study participants. KNHANES: Korea National Health and Nutrition Examination Surveys, AD: atopic dermatitis.

Table 1. Sociodemographic characteristics and comorbidities of study participants

Variable	Total	Non-AD	AD	p-value
Total population				
Number	21,606	21,043	563	
Percent (%)	100.0	96.69±0.40	3.31±0.40	
Sex				0.126
Male	49.62±1.11	49.50±1.11	53.34±1.11	
Female	50.38±1.11	50.50±1.11	46.66±1.11	
Age (yr)	46.89±14.69	47.20±14.57	35.31±14.45	<0.001*
Insurance type				0.644
Medical aid	2.30±0.33	2.28±0.33	2.64±0.36	
Health insurance	97.7±0.33	97.72±0.33	97.36±0.36	
Household income (quantile)				0.621
Low	11.41±0.71	11.47±0.71	9.8±0.66	
Mid-low	25.68±0.97	25.70±0.97	24.98±0.96	
Mid-high	31.27±1.03	31.18±1.03	33.85±1.05	
High	31.65±1.03	31.66±1.03	31.38±1.03	
Education				<0.001*
≤Primary school	12.13±0.72	12.38±0.73	4.56±0.46	
Middle school	8.84±0.63	8.97±0.63	5.07±0.49	
High school	40.66±1.09	40.25±1.09	52.60±1.11	
≥College	38.37±1.08	38.40±1.08	37.76±1.08	
Region				0.007*
Rural	27.43±0.99	27.64±0.99	21.52±0.91	
Urban	72.57±0.99	72.36±0.99	78.48±0.91	
BMI (kg/m^2)				0.118
Obese (≥30)	4.68±0.47	4.60±0.47	6.85±0.56	
Overweight	27.20±0.99	27.26±0.99	25.56±0.97	
Normal (<25)	68.12±1.03	68.14±1.03	67.59±1.04	
Alcohol consumption				<0.001*
None	20.73±0.9	20.95±0.9	14.33±0.78	
Occasionally (<2/wk)	56.54±1.1	56.21±1.1	66.24±1.05	
Frequently (≥2/wk)	22.73±0.93	22.84±0.93	19.43±0.88	
Smoking status				0.242
Current smoker	24.58±0.96	24.51±0.95	26.53±0.98	
Ex-smoker	19.69±0.88	19.79±0.88	16.55±0.82	
Non-smoker	55.73±1.1	55.69±1.1	56.92±1.1	
Asthma				<0.001*
No	97.27±0.36	97.45±0.35	91.93±0.6	
Yes	2.73±0.36	2.55±0.35	8.07±0.6	
Allergic rhinitis				<0.001*
No	83.89±0.82	84.46±0.8	67.03±1.04	
Yes	16.11±0.82	15.54±0.8	32.97±1.04	
Hypertension				<0.001*
No	87.07±0.74	86.77±0.75	95.71±0.45	
Yes	12.93±0.74	13.23±0.75	4.29±0.45	
Diabetes mellitus				<0.001*
No	95.10±0.48	94.99±0.48	98.13±0.3	
Yes	4.90±0.48	5.01±0.48	1.87±0.3	
Hyperlipidemia				0.008*
No	93.78±0.54	93.69±0.54	96.41±0.41	
Yes	6.22±0.54	6.31±0.54	3.59±0.41	

Values are presented as number only, mean±standard deviation, or weighted %±standard error. AD: atopic dermatitis, BMI: body mass index. p-values were calculated by design-based Wilcoxon rank-sum test for complex sample survey data or Pearson's χ^2 test with Rao–Scott adjustment (*$p<0.05$ is statistically significant).

urban areas ($p=0.007$), had more asthma patients ($p<0.001$), more patients with allergic rhinitis ($p<0.001$), lower prevalence of hypertension ($p<0.001$), lower prevalence of diabetes mellitus ($p<0.001$), and lower prevalence of hyperlipidemia ($p<0.001$) than the non-AD group. There was no statistically significant difference in the proportion of smokers, while the proportion of alcohol consumers was significantly different between the two groups. The oral health behaviors and nutritional habits data of the participants are shown in Table 2. There were significant differences in the frequency of tooth brushing and dietary behaviors between AD and non-AD participants.

The prevalence of DMFT was significantly higher in the AD group than in the non-AD group both in the simple logistic regression analysis ($p=0.025$) and the multiple logistic regression analysis after adjustment for sociodemographic characteristics (sex, region, household income, and education) and BMI (Model 1: OR, 1.58; 95% confidence interval [CI], 1.09~2.30; $p=0.015$). Particularly, even af-

ter adjusting for the effects of smoking status, alcohol consumption, oral health behaviors (frequency of tooth brushing, experience of dental check-up within 1 year, use of dental floss, interdental brush, and mouth wash) nutritional habits (frequency of intake of crackers/cookies, carbonated soft drinks, and ice-cream/sherbet), and comorbidities (allergic rhinitis, asthma, hypertension, diabetes mellitus, and hyperlipidemia), the OR was still statistically significant (Model 2: OR, 1.58; 95% CI, 1.08~2.29; $p=0.017$) (Table 3). In addition, when using the Poisson regression analysis, there was a significant difference in the mean ratio of the DMFT index between the AD and non-AD groups after adjustment (Model 2: mean ratio, 1.07; 95% CI, 1.00~1.14; $p=0.046$) (Table 4). However, the prevalence of the SiC group, which indicates severe dental caries, did not differ regardless of AD presence, and the proportion of participants who rated oral health status as poor were not significantly higher in the AD group than in the non-AD group (Table 3).

Table 2. Oral health behaviors and nutritional habits data

Variable	Total	Non-AD	AD	p-value
Frequency of tooth brushing				0.029*
≤1	10.20±0.67	10.31±0.68	7.02±0.57	
2	40.73±1.09	40.79±1.09	38.82±1.08	
≥3	49.07±1.11	48.90±1.11	54.16±1.11	
Dental check-up (≤1 year)				0.516
No	71.92±1.00	71.97±1.00	70.49±1.01	
Yes	28.08±1.00	28.03±1.00	29.51±1.01	
Use of dental floss				0.139
No	79.99±0.89	80.09±0.89	76.98±0.93	
Yes	20.01±0.89	19.91±0.89	23.02±0.93	
Use of interdental brush				0.877
No	85.46±0.78	85.47±0.78	85.2±0.79	
Yes	14.54±0.78	14.53±0.78	14.8±0.79	
Use of mouthwash				0.599
No	83.12±0.83	83.09±0.83	84.00±0.81	
Yes	16.88±0.83	16.91±0.83	16.00±0.81	
Frequency of food intake				
Crackers/cookies				0.001*
Almost none	8.46±0.62	8.58±0.62	5.09±0.49	
Occasionally (<2/wk)	72.99±0.99	73.05±0.98	71.13±1.01	
Frequently (≥2/wk)	18.55±0.86	18.37±0.86	23.78±0.94	
Carbonated soft drinks				<0.001*
Almost none	12.75±0.74	12.99±0.75	5.90±0.52	
Occasionally (<2/wk)	70.22±1.01	70.41±1.01	64.66±1.06	
Frequently (≥2/wk)	17.03±0.83	16.60±0.83	29.44±1.01	
Ice-cream/sherbet				<0.001*
Almost none	9.15±0.64	9.31±0.64	4.48±0.46	
Occasionally (<2/wk)	81.54±0.86	81.63±0.86	78.86±0.91	
Frequently (≥2/wk)	9.32±0.65	9.06±0.64	16.66±0.83	

Values are presented as %±standard error. AD: atopic dermatitis. p-values were calculated by using Pearson's χ^2 test with Rao–Scott adjustment (*$p<0.05$ is statistically significant).

Table 3. Prevalence and adjusted odds ratios for experience of dental caries, severe dental caries group and poor subjective oral status to atopic dermatitis in Korean adults

Variable	Prevalence (%±SE)			Unadjusted		Model 1		Model 2	
	Total	Non-AD	AD	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
DMFT index >0	89.75±0.67	89.64±0.68	92.92±0.57	1.52 (1.05~2.18)	0.025*	1.58 (1.09~2.30)	0.015*	1.58 (1.08~2.29)	0.017*
SiC group	30.35±1.02	30.41±1.02	28.66±1.00	0.92 (0.74~1.14)	0.434	1.04 (0.84~1.29)	0.727	1.04 (0.84~1.30)	0.713
Poor subjective oral status	56.36±1.10	38.99±1.08	61.02±1.08	1.22 (0.99~1.49)	0.053	1.06 (0.87~1.31)	0.530	1.05 (0.85~1.29)	0.661

Model 1: Adjusted for age, sex, region, household income, education, body mass index, Model 2: Model 1+smoking status, alcohol consumption, oral health behavior (frequency of tooth brushing, experience of dental check-up within 1 year, use of dental floss, interdental brush and mouth wash), nutritional habit (frequency of intake of crackers/cookies, carbonated soft drinks and ice-cream/sherbet), allergic rhinitis, asthma, hypertension, diabetes mellitus, hyperlipidemia, SE: standard error, AD: atopic dermatitis, OR: odds ratio, CI: confidence interval, DMFT: decayed, missed, and filled teeth, SiC: significant caries index. p-values were calculated by using the simple and multiple logistic regression analyses (*p<0.05 is statistically significant).

Table 4. Poisson regression analysis between atopic dermatitis and DMFT index in Korean adults

Condition	DMFT index (mean±SE)		Mean ratio (95% CI)	p-value
	Non-AD	AD		
Unadjusted	6.43±0.05	6.47±0.22	1.01 (0.94~1.08)	0.851
Model 1	6.42±0.05	6.85±0.23	1.07 (1.00~1.14)	0.055
Model 2	6.42±0.05	6.85±0.22	1.07 (1.00~1.14)	0.046*

Model 1: Adjusted for age, sex, region, household income, education, body mass index, Model 2: Model 1+smoking status, alcohol consumption, oral health behavior (frequency of tooth brushing, experience of dental check-up within 1 year, use of dental floss, interdental brush and mouth wash), nutritional habit (frequency of intake of crackers/cookies, carbonated soft drinks and ice-cream/sherbet), allergic rhinitis, asthma, hypertension, diabetes mellitus, hyperlipidemia, DMFT: decayed, missed, and filled teeth, SE: standard error, CI: confidence interval, AD: atopic dermatitis. p-values were calculated by using Poisson regression analyses (*p<0.05 is Statistically significant).

DISCUSSION

To the best of our knowledge, the present study is the first study to evaluate the association between dental caries and AD in an adult population, which was defined by self-reported physician diagnosis. In our study, AD was significantly associated with dental caries in Korean adults. The mean DMFT index was significantly higher in the AD group, indicating that the progression of dental caries may also be associated with AD, although the mean ratio of the DMFT index was marginal. Until now, the association between AD and dental caries has not been widely studied and has mainly been focused on children. Perugia et al.[12] carried out a single-center observational study, which reported the prevalence of dental caries (54.4%, 49/90) in children and adolescents who were clinically diagnosed with AD, but no statistical analysis was performed to compare this prevalence to that in the non-AD group. Recently, Kalhan et al.[13] conducted a longitudinal cohort study to examine the impact of AD on early childhood caries (ECC) development. They defined a childhood AD group whose parents reported that their children had been diagnosed with AD by a physician, and skin prick tests (SPT) were also performed for confirmation of the diagnosis. AD children with positive SPT showed a higher risk of ECC development at age 2 (adjusted OR, 3.29; 95% CI, 1.06~10.17; p=0.038) and 3 years (adjusted OR, 3.09; 95% CI, 1.24~7.17; p=0.015). An ectodermal defect during tissue development is suggested as a potential common pathogenic pathway of dental caries and AD, but neither the exact mechanism nor the direct causality was determined in this study.

According to a recent longitudinal twin cohort study in 6-year-old children, the overall concordance in the twin cohort was moderate (0.47; 95% CI, 0.32~0.62), indicating that either genetic or environmental shared factors play a role in the etiology of hypomineralization of the second molars (HSPM), but there was weak evidence of higher concordance for HSPM in monozygotic twins when compared to dizygotic twins (*p*=0.078)[18]. Of the confounding factors, infantile eczema contributed more than 2-fold relative odds for HSPM (adjusted OR, 2.05; 95% CI, 1.01~4.13; *p*=0.046), while the period when the second primary molars would be considered vulnerable to HSPM generally precedes the time at which infantile eczema occurs. These findings suggest that not only eczema itself, but also common developmental pathways could possibly be attributed to enamel hypomineralization, which is a risk factor for dental caries[19].

Among the multifactorial etiologies of dental caries, the host factors, particularly genetic ones, are considered to be risk factors for caries in AD patients. In a recent study, epithelial hair keratin gene (*KRT75*) polymorphisms were prone to increased enamel structure alterations, a possible connection between hair disorders and susceptibility to dental caries was demonstrated[20]. Similarly, the barrier abnormalities in AD, which are also caused by various genetic mutations, could play a role in the pathogenesis of caries[21]. The distal-less homeobox (*Dlx-3*) gene has been shown to play a crucial role in both enamel formation and regulation of epidermal differentiation; polymorphisms in *MBL2* and *TLR2* have also been associated with both AD and dental caries[22]. The filaggrin gene (*FLG*), which is expressed in both the skin and oral mucosa, also affects the pathogenesis of dental caries in AD patients[23]. Thus, the absence of filaggrin in the oral mucosa promotes epidermal barrier dysfunction, leading to dryness and infections caused by *Streptococcus mutans*, *Streptococcus sobrinus*, and *Lactobacilli*[12].

Mouth breathing is not only known to be associated with atopic diseases including allergic rhinitis and asthma, but is also revealed as one of the common characteristics in AD patients[24-26]. Breathing through the mouth results in an alteration in the defense mechanisms of oral tissues, as the mucosa is exposed to air during respiration, leading to an increased risk of cariogenic activity[27-30]. Koga-Ito et al.[31] found a high prevalence of *S. mutans* in 70% of mouth breathers and 43.3% of the controls, indicating a higher tendency for cariogenic activity.

As AD is a chronic relapsing cutaneous disorder, the majority of moderate to severe AD patients are treated with systemic corticosteroids, immunomodulators, and antihistamines. Long-term use of systemic corticosteroids is asso-

ciated with opportunistic oral infections by suppressing cellular immunity and phagocytosis[32]. Javad et al.[33] verified that *Candida albicans* was isolated from the oral cavity of 23% of AD patients and 6% of the healthy controls (*p*<0.05). Antihistamines cause decreased salivary flow and xerostomia due to antimuscarinic effects. As salivary flow plays an important role in the prevention of caries, antihistamines, which are frequently used drugs in AD, are also thought to be cariogenic drugs[34].

The limitations of this study are as follows. First, given the cross-sectional nature of the study, causality could not be inferred between AD and dental caries. Second, although the questionnaire used for self-reported AD has been validated for studying comorbidities of AD (specificity: 0.97, positive predictive value: 0.91), relatively low negative predictive value (0.70), and very poor sensitivity (0.43) may result in misclassifications, in which some participants who reported not having AD actually had the disease[15]. Third, the information about systemic treatments of AD and the severity of AD were not included as potentially related confounders. However, this is presumably the first study using nationally representative data that has comprehensively investigated a possible association between dental caries and AD. As such, we could minimize selection bias by using nationwide survey data. In addition, various other factors associated with caries, such as age, socioeconomic status, dietary data, and oral health behaviors, could be adjusted in the analysis.

In a nutshell, patients with AD had a significantly higher risk of developing dental caries than non-AD patients. Based on our study results, dermatologists should be aware of the dental manifestations of AD patients, and recommend regular dental check-ups for the early detection of caries. Further studies with prospective longitudinal study designs and more accurate diagnostic systems should be conducted to verify the direct role of AD in the development of caries. In addition, further research on the common developmental pathways between AD and enamel formation will provide insight into potential mechanisms underlying the association between dental caries and AD.

CONFLICTS OF INTEREST

FUNDING SOURCE

DATA SHARING STATEMENT

All the datasets from the present study may be obtained from the corresponding author upon request.

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REFERENCES

1. Kobayashi T, Glatz M, Horiuchi K, Kawasaki H, Akiyama H, Kaplan DH, et al. Dysbiosis and staphylococcus aureus colonization drives inflammation in atopic dermatitis. Immunity 2015;42:756-766.
2. Ong PY, Ohtake T, Brandt C, Strickland I, Boguniewicz M, Ganz T, et al. Endogenous antimicrobial peptides and skin infections in atopic dermatitis. N Engl J Med 2002;347:1151-1160.
3. Higaki S, Morohashi M, Yamagishi T, Hasegawa Y. Comparative study of staphylococci from the skin of atopic dermatitis patients and from healthy subjects. Int J Dermatol 1999;38:265-269.
4. Gong JQ, Lin L, Lin T, Hao F, Zeng FQ, Bi ZG, et al. Skin colonization by Staphylococcus aureus in patients with eczema and atopic dermatitis and relevant combined topical therapy: a double-blind multicentre randomized controlled trial. Br J Dermatol 2006;155:680-687.
5. Centers for Disease Control and Prevention. Oral health surveillance report: trends in dental caries and sealants, tooth retention, and edentulism, United States, 1999-2004 to 2011-2016. Atlanta: Centers for Disease Control and Prevention, 2019.
6. Namal N, Can G, Vehid S, Koksal S, Kaypmaz A. Dental health status and risk factors for dental caries in adults in Istanbul, Turkey. East Mediterr Health J 2008;14:110-118.
7. Nishi M, Harding M, Kelleher V, Whelton H, Allen F. Knowledge of caries risk factors/indicators among Japanese and Irish adult patients with different socio-economic profiles: a cross-sectional study. BMC Oral Health 2017;17:55.
8. Silva Junior MF, Batista MJ, de Sousa MDLR. Risk factors for tooth loss in adults: a population-based prospective cohort study. PLoS One 2019;14:e0219240.
9. Takahashi N, Nyvad B. The role of bacteria in the caries process: ecological perspectives. J Dent Res 2011;90:294-303.
10. Choi YY. Relationship between asthma and dental caries in Korean adults: data from the Sixth Korea National Health and Nutrition Examination Survey. J Korean Soc Dent Hyg 2019;19:131-140.
11. Ho SW, Lue KH, Ku MS. Allergic rhinitis, rather than asthma, might be associated with dental caries, periodontitis, and other oral diseases in adults. PeerJ 2019;7:e7643.
12. Perugia C, Saraceno R, Ventura A, Lorè B, Chiaramonte C, Docimo R, et al. Atopic dermatitis and dental manifestations. G Ital Dermatol Venereol 2017;152:122-125.
13. Kalhan TA, Loo EXL, Kalhan AC, Kramer MS, Karunakaran B, Un Lam C, et al. Atopic dermatitis and early childhood caries: results of the GUSTO study. J Allergy Clin Immunol 2017;139:2000-2003.
14. Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, Choi S, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014;43:69-77.
15. Silverberg JI, Patel N, Immaneni S, Rusniak B, Silverberg NB, Debashis R, et al. Assessment of atopic dermatitis using self-report and caregiver report: a multicentre validation study. Br J Dermatol 2015;173:1400-1404.
16. World Health Organization. Oral health surveys: basic methods. 5th ed. Geneva: World Health Organization, 2013.
17. World Health Organization (WHO). Oral health surveys. 5th ed. Geneva: WHO, 2013.
18. Silva MJ, Kilpatrick NM, Craig JM, Manton DJ, Leong P, Burgner D, et al. Etiology of hypomineralized second primary molars: a prospective twin study. J Dent Res 2019;98:77-83.
19. Mittal R, Chandak S, Chandwani M, Singh P, Pimpale J. Assessment of association between molar incisor hypomineralization and hypomineralized second primary molar. J Int Soc Prev Community Dent 2016;6:34-39.
20. Duverger O, Ohara T, Shaffer JR, Donahue D, Zerfas P, Dullnig A, et al. Hair keratin mutations in tooth enamel increase dental decay risk. J Clin Invest 2014;124:5219-5224.
21. Weidinger S, Novak N. Atopic dermatitis. Lancet 2016;387:1109-1122.
22. Nibali L, Di Iorio A, Tu YK, Vieira AR. Host genetics role in the pathogenesis of periodontal disease and caries. J Clin Periodontol 2017;44 Suppl 18:S52-S78.
23. De Benedetto A, Qualia CM, Baroody FM, Beck LA. Filaggrin expression in oral, nasal, and esophageal mucosa. J Invest Dermatol 2008;128:1594-1597.
24. Yamaguchi H, Tada S, Nakanishi Y, Kawaminami S, Shin T, Tabata R, et al. Association between mouth breathing and atopic dermatitis in Japanese children 2-6 years old: a population-based cross-sectional study. PLoS One 2015;10:e0125916.
25. Izuhara Y, Matsumoto H, Nagasaki T, Kanemitsu Y, Murase K, Ito I, et al. Mouth breathing, another risk factor for asthma: the Nagahama Study. Allergy 2016;71:1031-1036.
26. Barros JR, Becker HM, Pinto JA. Evaluation of atopy among mouth-breathing pediatric patients referred for treatment to a tertiary care center. J Pediatr (Rio J) 2006;82:458-464.
27. Elad S, Heisler S, Shalit M. Saliva secretion in patients with allergic rhinitis. Int Arch Allergy Immunol 2006;141:276-280.
28. Lenander-Lumikari M, Laurikainen K, Kuusisto P, Vilja P. Stimulated salivary flow rate and composition in asthmatic and non-asthmatic adults. Arch Oral Biol 1998;43:151-156.
29. Wongkamhaeng K, Poachanukoon O, Koontongkaew S. Dental caries, cariogenic microorganisms and salivary pro-

perties of allergic rhinitis children. Int J Pediatr Otorhinolaryngol 2014;78:860-865.

30. l-Awadi RN, Al-Casey M. Oral health status, salivary physical properties and salivary Mutans Streptococci among a group of mouth breathing patients in comparison to nose breathing. J Bagh Coll Dent 2013;25:152-159.

31. Koga-Ito CY, Unterkircher CS, Watanabe H, Martins CA, Vidotto V, Jorge AO. Caries risk tests and salivary levels of immunoglobulins to Streptococcus mutans and Candida albicans in mouthbreathing syndrome patients. Caries Res 2003;37:38-43.

32. Araujo MR, Grégio AMT, Azevedo LR, Machado MÂN, Mattioli T, Castro LFÁ. [Adverse drug effects of dental interest]. Rev Odontol Arac 2005;26:28-33. Portuguese.

33. Javad G, Taheri Sarvtin M, Hedayati MT, Hajheydari Z, Yazdani J, Shokohi T. Evaluation of candida colonization and specific humoral responses against candida albicans in patients with atopic dermatitis. Biomed Res Int 2015;2015: 849206.

34. Scully C. Drug effects on salivary glands: dry mouth. Oral Dis 2003;9:165-176.