Allergic rhinitis, rather than asthma, is a risk factor for dental caries, periodontitis, and other oral diseases in adults (#36547)

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Allergic rhinitis, rather than asthma, is a risk factor for dental caries, periodontitis, and other oral diseases in adults

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Background: Several studies have found an association between asthma (AS) and oral disease. In children, allergic rhinitis (AR), rather than AS is a risk factor for dental caries was reported. In adult, whether the association of AS and oral disease comes from AR, a co-confounder, requires further research.

Methods: Data from 22,898 men and 28,541 women, aged 21 to 25 years, were collected from a national database in Taiwan. Individuals were separated into those with AR versus non-AR groups and AS versus non-AS groups. Five common oral diseases were studied: dental caries, periodontitis, pulpitis, gingivitis, and stomatitis/aphthae. We analyzed disease rates between groups and for different demographic characteristics. The frequencies of clinical visit times and impact of topical steroid use between groups were also studied. AR was adjusted for when studying the association between AS and oral disease, and AS was adjusted for when studying the association between AR and oral disease.

Results: After adjusting for confounding factors and AS, the rate and frequencies of clinical visits for all five oral diseases were higher in those with AR. AS was associated with oral disease after adjusting for confounding factors; however, if AR was included for adjustment, no relationship was found between AS and oral disease. In AR group, males, those with higher incomes, and country residents had a high risk of developing oral disease. Intranasal steroids, rather than inhaled steroids, are associated with oral disease.

Conclusion: Among young adults, it is AR, rather than AS, that is a risk factor for oral disease.

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Abstract

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Introduction

Dental caries, periodontitis, pulpitis, gingivitis, and stomatitis/aphthae are common oral diseases (Frencken et al 2017), which have a negative impact on quality of life and work performance and increase medical costs. Understanding the risk factors for these conditions may help in prevention and treatment. Asthma (AS) and allergic rhinitis (AR) are common chronic diseases, with complications – such as mouth breathing, and changes in oral flora and saliva – which are also risk factors for oral disease and may increase its prevalence (Mummolo et al 2018; Wongkamhaeng ea al 2014).

A growing number of studies have indicated that AS significantly increases the risk of caries (Alavaikko et al 2011), periodontitis, and gingivitis (Moraschini et al 2018). AR and AS often coexist (Simons 1999), and an association has also been reported between AR, caries, and periodontitis (Hung SH et al 2016; Bakhshaee et al 2017). However, AR was never considered to be a confounder in the studies about AS and oral disease. Our previous study found that, in children, AR – rather than AS – is a risk factor for dental caries (Chuang et al 2018). The co-confounder, AR, brings the relationship between AS and caries into question. We speculate that, as with the study results in children, AR – rather than AS –might be the causal factor in oral disease in adults.

Studies on the association of AR with caries and periodontitis are few, and they also have conflicting results (Wongkamhaeng ea al 2014; Hung SH et al 2016; Bakhshaee et al 2017; Kim et al 2018). The association between AS and pulpitis and stomatitis, and between AR and pulpitis, gingivitis, and stomatitis have scarcely been studied. Using the National Health Insurance Research Database (NHIRD) in Taiwan, we performed a large longitudinal,

population-based research study to establish the relationship/s among the five oral diseases of caries, periodontitis, pulpitis, gingivitis, and stomatitis/aphthae, and AS and AR in young adults. AR was adjusted for when studying the association between AS and oral disease; we aimed to determine whether the association was induced by AR, the co-confounder.

Materials & Methods

Database and data collection

The NHIRD was created by the National Health Research Institute (NHRI) in Taiwan (Department of health, E. Y. 1998; Cheng 2003). The NHRI randomly sampled a representative database of 1 million subjects in 2010 through systematic sampling, and this sample served as our data source. The database provides information on patient identification, birth date, sex, diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems (ICD)-9-CM, prescription drugs, medical care facilities, and other items.

Criteria for AS, AR and oral disease

Subjects born between 1985 and 1988 were randomly selected from the NHIRD. During years 2005 to 2013, their claims data from the ages of 21 to 25 years were analyzed. The subjects were divided into the following groups: AR and non-AR, and AS and non-AS. The criteria for AR and AS were as follows: at least two diagnoses of AR (ICD-9-CM diagnostic code 477) or AS (ICD-9-CM diagnostic code 493) in the 5 years between the ages of 21 and 25 years. Because AR and AS are chronic diseases, those with disease durations of AR and AS <180 days were excluded. Five major oral diseases were selected for our study: dental caries (code 521.0), periodontitis (codes 523.3 and 523.4), pulpitis (code 522.0), gingivitis (codes 523.0 and 523.1), and stomatitis (code 528.0)/oral aphthae (code 528.2).

106

107 **Rate of oral disease**

108 Rates of the five oral diseases in the AR versus non-AR groups and AS versus non-AS
109 groups were compared. More than one diagnosis of each oral disease recorded within the 5 years
110 was defined as having the individual disease. The influence of AR on oral disease according to
111 various demographic characteristics was compared, including male versus female, urban versus
112 country resident, and high versus low income. The magnitude of the oral diseases' odds ratio
113 (OR) between AR and non-AR subjects was used for comparison.

114

115 **Clinical visit times for oral disease**

116 For the 5 years, the mean clinical visit times for the five oral diseases in the various groups
117 were compared. Mean clinical visit times for three dental treatment methods – dental restoration,
118 endodontics, and periodontitis treatment (surgical and non-surgical) – were also compared.

119

120 **Influence of use of inhaled steroids for AS and intranasal steroids for AR**

121 AR subjects were divided into those who had ever used intranasal steroids in the 5 years
122 (intranasal steroid group) and those who had never used intranasal steroids in the 5 years (non-
123 intranasal steroid group). AS subjects were divided into those who had ever used inhaled steroids
124 in the past 5 years (inhaled steroid group) and those who had never used inhaled steroids in the 5
125 years (non-inhaled steroid group). Clinical visit times and treatments for oral disease were
126 compared between groups. Anatomical Therapeutic Chemical code R01AD was used for
127 intranasal steroids, and R03AK and R03BA for inhaled steroids.

128

Determining confounding factors

Factors that influence oral health include socioeconomic status, and urbanization. Socioeconomic status was defined according to occupation, which was grouped into high-income (teacher or public official, company employee) and low-income (other, peasants or fisherman, low income or no fixed job). Based on Liu's report (Chieh et al. 2006), urbanization levels were grouped into seven levels: levels 1-2 for urban residents, and levels 3-7 for country residents.

Factors that influence oral disease include dentofacial anomalies (ICD-9-CM code 524), salivary flow diseases (ICD-9-CM codes 527 and 710.2), diabetes mellitus (DM) (ICD-9-CM code 250) and esophageal reflux (ICD-9-CM codes 530.11 and 530.81).

All of the factors mentioned above, as well as sex, pregnancy, and obesity (ICD-9-CM code 278) were considered as risk factors and were adjusted for. When investigating the association between AR and oral disease, AS was viewed as the confounding factor, and when investigating the association between AS and oral disease, AR was viewed as the confounding factor.

Statistical analysis

All analyses were performed using SAS version 9.1 for Windows (SAS Inc., Cary, NC, United States of America (USA)) and PASW Statistics 18 (IBM, Armonk, NY, USA). The chi-square test was used to compare the rate of oral disease between groups. Multivariate regression analyses were used for adjusting the confounding factors (sex, socioeconomic status, urbanization, dentofacial anomalies, diseases of salivary flow, obesity, DM, esophageal reflux, pregnancy, AS, AR). The t-test was used for assessing differences in the frequencies of oral disease and clinical treatment visits between groups. Multivariate logistic regression and

multivariate regression analyses were used for adjusting for confounding factors. Two-sided *p* values of < 0.05 were defined as significant.

Results

Demographic data

In total 51,439 subjects were recruited, of whom 22,898 (44.5%) were men and 28,541 (55.5%) were women. Of these subjects, 7,884 (15.3%) fell into the AR group (3,247 (14.2%) men and 4,637 (16.2%) women), while 1,232 (2.4%) were AS subjects (569 (2.5%) men and 663 (2.3%) women).

Rates of oral diseases

The results for rates of oral diseases are presented in Table 1. Rates of the five oral diseases were all higher in AR subjects compared to non-AR subjects, and this difference was statistically significant. The statistical significance was still noted if AS was added for adjustment. The rates of caries, periodontitis, gingivitis, and aphthae/stomatitis were higher in AS subjects than in non-AS subjects, and this difference was also statistically significant. However, if AR was added for adjustment, the differences all became non-significant.

The magnitude of ORs for oral diseases in AR and non-AR subjects with different demographic characteristics were compared (Table 2). AR males had higher rates of caries (ORs: 1.78 for males, 1.68 for females) and aphthae/stomatitis (ORs: 1.76 for males, 1.65 for females) than AR females. AR country residents had higher rates of the five oral diseases (higher ORs) than AR urban residents, and AR subjects with high incomes had higher rates of the five oral diseases (higher ORs) than AR subjects with low incomes.

174

175 **Clinical visits for oral diseases and treatment**

176 Mean clinical visit times for the five oral diseases and three treatments in the 5 years were
177 significantly higher in AR subjects (Table 3), and the statistical significance was still noted if AS
178 was added for adjustment. Except for endodontics treatment, mean clinical visit times for five
179 oral diseases and two treatments were significantly higher in AS subjects; however, if AR was
180 added for adjustment, the differences all became non-significant.

181

182 **Association between inhaled steroids, intranasal steroids and oral disease**

183 The results for this association are presented in Table 4. In AR subjects, mean clinical visit
184 times for caries, periodontitis, gingivitis, periodontitis treatment and restoration treatment were
185 significantly higher in those using intranasal steroids, and the statistical significance was still
186 noted after adjustment for AS. In AS subjects, there was no significant association between mean
187 clinical visit times for oral diseases and treatments of those who inhaled steroids and those who
188 did not.

189 ## Discussion

190 Studies on the relationship between AR and caries reveal conflicting results: some studies
191 found a positive association (Bakhshaee et al 2017; Chuang et al 2018), while others found no
192 association (Wongkamhaeng ea al 2014; Tanaka et al 2008). No studies were reported in adults.
193 The relationship between AR and periodontitis is inconclusive, because both positive (Hung SH
194 et al 2016) and inverse (Kim et al 2018) associations have been reported. To the best of our
195 knowledge, an association between AR and gingivitis, pulpitis, and stomatitis/aphthae has not
196 previously been reported.

Our study provides evidence that AR is associated with five oral diseases (caries, periodontitis, pulpitis, gingivitis, and stomatitis/aphthae). The increased prevalence rate means that AR might influence development of oral diseases, while increased clinical visit times mean that AR might increase the severity of oral diseases. Restoration and endodontics treatment are used for caries, periodontitis, and pulpitis, and increased treatment visit times in AR subjects makes the association more certain. Among the AR subjects, males, country residents and those with high income had higher ORs for oral diseases. This tells us that males who are country residents with a high income should pay more attention to their oral health if they also have AR.

There have been more studies investigating the association between AS and caries, periodontitis and gingivitis, than on the association with AR. Not all, but more and more studies are finding a positive association between AS, caries (Alavaikko et al 2011), periodontitis and gingivitis (Moraschini et al 2018). However, most of the studies did not adjust for AR, which is an important confounder. In our study, before adjusting for AR, rates for four oral diseases (Table 1), and clinical visit times for five oral diseases and three oral treatments were significantly higher in AS subjects. However, after adjusting for AR, the differences were all non-significant. We concluded that AS is not associated with oral disease. AR might be a co-confounder that is associated with both AS and oral disease. The finding of an association between AS and oral disease comes from the co-cofounder: AR.

Inhaled steroids were reported to increase the rate of caries, periodontitis, gingivitis and oral ulcers, with change in oral pH, local deposition of steroids in the oral cavity, and their effect on oral mucosa being the mechanisms (Alavaikko et al 2011; Bozejac et al 2017). The study of intranasal steroids and oral disease is limited. We speculate that local deposition of steroids due to postnasal dripping might induce the same oral diseases that inhaled steroids do. In our study,

three oral diseases and two oral treatment visit times were significantly associated with use of intranasal steroids, but no association was noted between inhaled steroids and oral disease (Table 4). Intranasal steroids are more expensive than inhaled steroids in Taiwan, so these drugs are prescribed if patients have more severe AR symptoms. More studies are necessary to explain our findings.

The results of several studies could explain the association between AS, AR, and oral disease. At the mechanical level, a decreased saliva secretion rate was reported in both AS (Lenander et al 1998) and AR (Elad et al 2006) subjects. Dehydration of the gingiva due to mouth breathing in AR subjects may also be a contributing factor for gingivitis. At the pharmacological level, antihistamines (Elad et al 2006) and inhaled β_2-agonists (Tootla et al 2004) could decrease salivary flow. At the microbiological level, AS (Sachs et al 1993) and AR (Wongkamhaeng ea al 2014) subjects were found to have different oral micro-flora than other subjects. At the immunological level, decreased IgA levels in gingival tissue have been reported in allergic disease (Ostergaard 1997), and IgA is a first-line defense immunoglobulin for mucosa, and plays a role in restricting periodontal disease. Another study indicated that interleukin (IL)-12 is associated with AR (Ping et al 2015); IL-12 may be related to the pathogenesis of periodontal disease (Tsai IS et al 2005).

Our study has several strengths. First, most previous studies have had a cross-sectional design; however, because caries, periodontitis, AR, and AS are chronic and changeable diseases, a longitudinal survey is better. Second, most of the cohort studies contain fewer subjects – our study contains 51,349 subjects, including 7,884 with AR and 1,232 with AS. This large national survey is also representative of the general population in Taiwan. Third, in other studies, AR or AS is assessed from past history, rather than being an existing condition at the time of study.

With more than two diagnoses within the 5 study years, AR and AS subjects in our study were in the active stage of allergic disease. Studying the association between oral disease and AR and AS during the allergic diseases' active stage is more pertinent. Fourth, by knowing the frequencies of clinical visits and treatment times, we could understand the influence of allergic disease on the severity of oral diseases, medical treatment and medical costs.

There are limitations to our study. First, there are no data on oral pathogenic bacteria. Second, although we adjusted for obesity, there are no data on sugar consumption. Third, there are no data on smoking, personal oral hygiene, oral drugs, and laboratory results.

Conclusions

The present study provides evidence that AR significantly increases the risk of caries, periodontitis, pulpitis, gingivitis, and stomatitis/aphthae in young adults. Based on increased clinical visit times for the five diseases, it can be speculated that AR also increases the severity of these five oral diseases. Contrary to findings in other studies, there is no association between AS and the five oral diseases. Any association between AS and oral diseases previously found might due to AR, the co-confounder.

Males who live in the countryside and have a high income should pay more attention to oral hygiene if they also have AR, because rates of the oral diseases were found to be higher in these demographic categories. Intranasal steroids used in AR – rather than inhaled steroids used in AS – are associated with the development of oral diseases.

In order to prevent and treat oral disease, simultaneously treating AR is important. In the study of the etiology of oral disease, considering the effects of AR is a new direction of study. However, more biological research and more epidemiological data on the relationship between AR, AS and oral disease are necessary in order to gain clarity on it.

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Table 1(on next page)

Tables

Tables

Table 1: The rates of oral disease in AR vs. non-AR and AS vs. non-AS subjects

	AR	Non-AR	OR (95% CI)	*p*-value (a)	*p*-value (b)
	n = 7,884(15.3%)	n = 43,555 (84.7%)			
Caries (%)	79.7%	69.1%	1.76(1.66~1.86)	<0.001	<0.001
Periodontitis (%)	71.5%	59.9%	1.69(1.60~1.78)	<0.001	<0.001
Pulpitis	25.7%	23.2%	1.15(1.09~1.21)	<0.001	<0.001
Gingivitis (%)	60.5%	49.5%	1.57(1.49~1.65)	<0.001	<0.001
Aphthae/stomatitis (%)	29.7%	19.8%	1.71(1.62~1.81)	<0.001	<0.001
	AS	Non-AS	OR (95% CI)	*p*-value (a)	*p*-value (c)
	n = 1,232(2.4%)	n = 50,207(97.6%)			
Caries (%)	76.8%	70.6%	1.38(1.21~1.58)	<0.001	0.152
Periodontitis (%)	67.8%	61.5%	1.32(1.17~1.49)	<0.001	0.358
Pulpitis	25.5%	23.5%	1.11(0.98~1.27)	0.246	0.608
Gingivitis (%)	57.7%	51.0%	1.31(1.17~1.49)	<0.001	0.140
Aphthae/stomatitis (%)	27.2%	21.2%	1.39(1.22~1.58)	<0.001	0.190

(a). Adjusted by sex, socioeconomic status, urbanization, dentofacial anomalies, disease of salivary flow, obesity, DM, esophageal reflux, pregnancy

(b). Adjusted by factors (a) plus AS

(c). Adjusted by factors (a) plus AR

Table 2: ORs between AR and non-AR groups, for the five oral diseases in males vs. females, urban vs. country residents, and subjects with high income vs. those with low income

	Male, n = 22,898 AR (14.2%) vs non-AR (85.8%)	Female, n = 28,541 AR (16.2%) vs non-AR (83.8%)
	OR (95% CI)	OR (95% CI)
Caries	1.78(1.64~1.94)	1.68(1.55~1.82)
Periodontitis	1.66(1.53~1.79)	1.67(1.56~1.80)
Pulpitis	1.12(1.02~1.22)	1.15(1.07~1.23)
Gingivitis	1.57(1.45~1.69)	1.53(1.44~1.64)
Aphthae/stomatitis	1.76(1.61~1.92)	1.65(1.54~1.77)
	Urban resident, n = 29,955 AR (15.8%) vs. non-AR (84.8%)	Country resident, n = 21,484 AR (14.7%) vs. non-AR (85.3%)
	OR (95% CI)	OR (95% CI)
Caries	1.64(1.52~1.77)	1.91(1.75~2.10)
Periodontitis	1.61(1.50~1.72)	1.79(1.85~1.95)
Pulpitis	1.10(1.02~1.18)	1.23(1.13~1.34)
Gingivitis	1.48(1.39~1.57)	1.697(1.57~1.83)
Aphthae/stomatitis	1.64(1.53~1.76)	1.82(1.67~1.98)
	High income, n = 28,776 AR (15.6%) vs. non-AR (84.4%)	Low income, n = 22,663 AR (14.9%) vs. non-AR (85.1%)
	OR (95% CI)	OR (95% CI)
Caries	1.90(1.75~2.05)	1.59(1.46~1.74)
Periodontitis	1.79(1.67~1.92)	1.56(1.45~1.69)
Pulpitis	1.17(1.10~1.27)	1.12(1.03~1.21)
Gingivitis	1.60(1.49~1.70)	1.53(1.42~1.65)
Aphthae/stomatitis	1.73(1.61~1.86)	1.69(1.56~1.83)

Table 3: Mean clinical visit times (over 5 years) for oral disease and treatments, for AR vs. non-AR and AS vs. non-AS subjects

	AR	Non-AR	Ratio	*p*-value (a)	*p*-value (b)
	n = 7,884 (15.3%)	n = 43,555 (84.7%)			
Caries	3.91	3.08	1.27	<0.001	<0.001
Periodontitis	2.16	1.61	1.34	<0.001	<0.001
Pulpitis	0.55	0.48	1.15	<0.001	0.001
Gingivitis	1.42	1.04	1.37	<0.001	<0.001
Aphthae/stomatitis	0.60	0.35	1.71	<0.001	<0.001
Periodontitis treatment	6.70	5.08	1.32	<0.001	<0.001
Restoration	7.45	6.05	1.23	<0.001	<0.001
Endodontics	1.79	1.62	1.10	0.003	0.006
	AS	Non-AS	Ratio	*p*-value (a)	*p*-value (c)
	n = 1,232(2.4%)	n = 50,207(97.6%)			
Caries	3.60	3.20	1.13	0.003	0.665
Periodontitis	1.94	1.69	1.15	0.002	0.898
Pulpitis	0.58	0.49	1.18	0.033	0.135
Gingivitis	1.32	1.09	1.21	<0.001	0.091
Aphthae/stomatitis	0.52	0.39	1.33	0.002	0.533
Periodontitis treatment	6.09	5.31	1.15	0.002	0.566
Restoration	7.03	6.24	1.13	0.001	0.324
Endodontics	1.82	1.64	1.11	0.166	0.379

(a). Adjusted by sex, socioeconomic status, urbanization, dentofacial anomalies, disease of salivary flow, obesity, DM, esophageal reflux, pregnancy

(b). Adjusted by factors (a) plus AS

(c). Adjusted by factors (a) plus AR

Table 4: Mean clinical visit times (over 5 years) for oral disease and treatments for AR subjects who had used intranasal steroids vs. those who never had, and AS subjects who had used inhaled steroids vs. those who never had

	AR (intranasal steroids)	AR (non-intranasal steroids)	Ratio	*p*-value (a)	*p*-value (b)
	n = 3,041 (38.6%)	n = 4,843 (61.4%)			
Caries	4.18	3.74	1.12	<0.001	<0.001
Periodontitis	2.28	2.09	1.09	0.002	0.001
Pulpitis	0.57	0.54	1.06	0.267	0.289
Gingivitis	1.53	1.35	1.13	<0.001	<0.001
Aphthae/stomatitis	0.64	0.57	1.12	0.129	0.130
Periodontitis treatment	7.08	6.46	1.10	<0.001	<0.001
Restoration	7.83	7.21	1.09	<0.001	<0.001
Endodontics	1.85	1.75	1.06	0.215	0.236
	AS (inhaled steroids)	AS (non-inhaled steroids)	Ratio	*p*-value (a)	*p*-value (c)
	n = 683 (55.4%)	n = 549 (44.6%)			
Caries	3.44	3.73	0.92	0.169	0.100
Periodontitis	1.99	1.90	1.05	0.581	0.787
Pulpitis	0.58	0.57	1.02	0.977	0.952
Gingivitis	1.25	1.39	0.90	0.140	0.059
Aphthae/stomatitis	0.48	0.55	0.87	0.276	0.112
Periodontitis treatment	6.06	6.12	0.99	0.722	0.321
Restoration	6.97	7.07	0.99	0.902	0.428
Endodontics	1.89	1.76	1.07	0.648	0.693

(a). Adjusted by sex, socioeconomic status, urbanization, dentofacial anomalies, disease of salivary flow, obesity, DM, esophageal reflux, pregnancy

(b). Adjusted by factors (a) plus AS

(c). Adjusted by factors (a) plus AR