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ORIGINAL ARTICLE

Dental Caries and Allergic Disorders in Japanese Children: The Ryukyus Child Health Study

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Background. Dental caries is an infectious disease and is highly prevalent among children. In the etiology of allergic diseases, the hygiene hypothesis contends that infections might confer protection against the development of allergic diseases. The aim of this cross-sectional study was to investigate the association between dental caries and the prevalence of allergic disorders. **Methods.** Study subjects were 21,792 children 6 to 15 years of age in Okinawa, Japan. Outcomes were based on diagnostic criteria from the International Study of Asthma and Allergies in Childhood. Data on dental caries were obtained from school records. Children were classified as having dental caries if one or more teeth had decayed and/or had been filled. Adjustment was made for sex, age, region of residence, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level. **Results.** The prevalence of wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months was 10.8%, 7.6%, 6.8%, and 7.6%, respectively. In an overall analysis, no measurable relationship was found between dental caries and the prevalence of wheeze, asthma, atopic eczema, or allergic rhinoconjunctivitis. However, dental caries was significantly inversely associated with the prevalence of allergic rhinoconjunctivitis only among children with a positive parental allergic history: The adjusted odds ratio was 0.84 (95% confidence interval: 0.72, 0.99). **Conclusions.** The present findings do not support the hypothesis that dental caries was protective against allergic diseases. However, a parental allergic history may affect the association between dental caries and allergic rhinoconjunctivitis.

Keywords asthma, caries, eczema, rhinitis, wheeze

INTRODUCTION

The prevalence of allergic disease in many countries, including Japan, has shown a dramatic increase in recent decades (1). The reasons for this increasing trend have not yet been clarified, but the hygiene hypothesis has been suggested as a possible explanation (2). According to this theory, growing up in a more hygienic environment with less microbial exposure might predispose to an increased risk of allergic diseases. Conflicting results have emerged from epidemiological studies attempting to associate infections with allergic diseases, however (3–10). In a German birth cohort, the number of viral infections in the first 3 years of life was inversely associated with the risk of wheeze at age 7 years, whereas repeated lower respiratory tract infections in the first 3 years of life showed a positive association with asthma and wheeze at 7 years of age (3). A US birth cohort study found that ear infections in the first years of life were inversely associated with atopy at school age (4). Several studies reported that there was no association between infectious diseases such as recurrent

upper respiratory tract infections, mumps, or rubella and allergic diseases and atopy (5–7). The association between infections and the development of allergic diseases might be influenced by many factors (8). These factors comprise various allergic illnesses including different phenotypes, timing of the exposure, various environmental exposures, and a subject's genetic susceptibility to react to these exposures (4, 11).

The major oral diseases are dental caries and periodontitis. These are local oral infectious diseases that are caused by the bacterial biofilm (dental plaque) that accumulates on teeth (12, 13). To our knowledge, only two cross-sectional studies have addressed that association between periodontal disease or oral bacteria and allergic diseases (14, 15). One study found an inverse association of periodontal disease with hay fever and house dust mite allergy, but not asthma, among German adults 20 to 79 years of age (14). In a US study, higher concentrations of serum immunoglobulin (IgG) antibodies to oral bacteria in relation to periodontal disease were significantly associated with lower prevalence of asthma, wheeze, and hay fever (15). Thus, it seems reasonable to assume a possible link between oral infectious diseases and allergic disorders. We hypothesized that dental caries may be inversely associated with allergic disorders. The aim of this study was to investigate the association between dental caries and the prevalence of wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis by using data from the Ryukyus Child

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Health Study (RYUCHS) and the school records of dental examinations.

METHODS

Study Population

Okinawa Prefecture is an island located in the southernmost area in Japan, with a subtropical climate and a total population of almost 1,375,000. Naha City, the largest city in Okinawa Prefecture and located in the south of the island, and Nago City, located in the center of the island, with a total population of almost 316,000 and 60,000, respectively, are 2 of the 41 municipalities in Okinawa Prefecture. During the period from September 2004 to January 2005, we conducted a cross-sectional school-based survey to investigate the associations between various selected factors and child health problems. All 35 public elementary schools and 17 junior high schools in Naha City and 17 public elementary schools and 8 junior high schools in Nago City participated in the RYUCHS. A set of 2 self-administered questionnaires was distributed by teachers to all 38,212 children at school. These were completed at home by parents of the elementary schoolchildren and the junior high school students themselves and/or their parents. Our research technicians checked the returned questionnaires according to the survey protocol. When missing answers and/or illogical data were detected, the teachers sent the questionnaires back to the parents. Finally, 28,885 sets of questionnaires were returned (participation rate = 75.6%). Permission to perform the RYUCHS was obtained from the ethics committee of the Faculty of Medicine, Fukuoka University.

Questionnaires

One of the questionnaires included questions regarding wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months based on the validated International Study of Asthma and Allergies in Childhood (ISAAC) phase-I questionnaire (16). We translated these questions into Japanese by using standard forward-backward translation. The definition of wheeze used in this study was determined by a positive response to the question, "Have you (Has your child) had wheezing or whistling in the chest in the last 12 months?" A positive response to both the aforementioned question and another question "Have you (Has your child) ever had asthma?" were considered to indicate asthma. For atopic eczema, affirmative answers to all of the following three questions in the ISAAC questionnaire were required: (1) "Have you (Has your child) ever had an itchy rash which was coming and going for at least 6 months?" (2) "Have you (Has your child) had this itchy rash at any time in the last 12 months?" and (3) "Has this itchy rash at any time affected any of the following places: the folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?" Allergic rhinoconjunctivitis was defined as a positive response to the following two questions: (1) "In the last 12 months, have you (Has your child) had a problem with sneezing or running or blocked nose when you (he/she) did not have a cold or flu?" and (2) "In the last 12 months, has this nose problem been accompanied by itchy-watery eyes?" The questionnaire also included questions about sex, age, number of siblings, paternal and maternal history of asthma,

atopic eczema, and allergic rhinitis, paternal and maternal educational level, and smoking in the household. A paternal or maternal history of asthma, atopic eczema, or allergic rhinitis was defined as positive if the respective parent had contracted any of these allergic disorders before the start of the survey.

The second questionnaire was a validated self-administered brief diet history questionnaire. Data regarding diet were not used in the current study.

Oral Examination

In Japan, an oral examination is conducted annually in schoolchildren under the School Health Law. A school dentist performs the oral examination by direct inspection. Oral measurements include the number of present, treated, and untreated teeth and assessment of the gingival condition and oral hygiene status. Radiographs are not performed. These data are forwarded to the Municipal Board of Education from each school. The data regarding dental examinations performed in 2004 were obtained from the Naha City Municipal Boards of Education and the Nago City Municipal Boards of Education. We combined the data from the oral examinations and the RYUCHS. Of the 28,885 children who took part in the RYUCHS, 27,202 were successfully linked. A total of 5,410 children were excluded because of missing or illogical data on variables under study, leaving data on 21,792 children available for analysis (57.0% of all eligible children). Children were classified as having dental caries if one or more teeth had decayed and/or had been filled. The present study was approved by the personal information protection committees of the Government of Naha City and the Government of Nago City.

Statistical Analysis

Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) for allergic disorders relative to dental caries. Adjusted ORs and 95% CIs were estimated using multiple logistic regression analysis. The following potential confounders were identified a priori and were included in the multivariate model: sex, age, region of residence, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level. Age was classified into three categories (6 to 8, 9 to 11, and 12 to 15 years of age), region of residence into two (Naha City and Nago City), number of siblings into four (0, 1, 2, and 3+), smoking in the household into three (never, former, and current), and paternal and maternal educational level into four (junior high school, high school, junior college or vocational technical school, and university). All statistical analyses were performed by using the SAS software package version 9.1 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

The prevalence values for symptoms of wheeze, asthma, atopic eczema, and allergic rhinoconjunctivitis in the previous 12 months were 10.8%, 7.6%, 6.8%, and 7.6%, respectively.

The distribution of selected factors under study is presented in Table 1. Approximately 60% of the subjects had two or

TABLE 1.—Distribution of selected characteristics in 21,792 schoolchildren, RYUCHS, Japan.

Variable	n (%)
Male sex	10,763 (49.4)
Age (y)	
6–8	6389 (29.3)
9–11	7926 (36.4)
12–15	7477 (34.3)
Region of residence	
Naha City	18,047 (82.8)
Nago City	3745 (17.2)
Siblings	
0	1986 (9.1)
1	7267 (33.4)
2	8311 (38.1)
3+	4228 (19.4)
Smoking in household	
Never	9411 (43.2)
Former	2237 (10.3)
Current	10,144 (46.6)
Paternal history of asthma	1495 (6.9)
Paternal history of atopic eczema	574 (2.6)
Paternal history of rhinitis	3762 (17.3)
Maternal history of asthma	1852 (8.5)
Maternal history of atopic eczema	978 (4.5)
Maternal history of rhinitis	4733 (21.7)
Paternal educational level	
Junior high school	1640 (7.5)
High school	9715 (44.6)
Junior college or vocational technical school	3247 (14.9)
University	7190 (33.0)
Maternal educational level	
Junior high school	1081 (5.0)
High school	9591 (44.0)
Junior college or vocational technical school	9418 (42.0)
University	1972 (9.1)
Dental caries experience	17,888 (82.1)

RYUCHS-Ryukyus Child Health Study.

more siblings. About half were exposed to household smoking at the time of the survey. Many more children had parents with a history of allergic rhinitis than parents with a history of asthma or atopic eczema. Approximately 80% of the children had dental caries. The mean number of carious teeth was 4.3 (standard deviation 3.5).

TABLE 2.—Crude and adjusted ORs and 95% CIs for allergic disorders according to dental caries experience among 21,792 schoolchildren, RYUCHS, Japan.

	Decayed and/or filled teeth	
	None	≥ 1
Wheeze		
Prevalence	437/3904 (11.2%)	1919/17,888 (10.7%)
Crude OR (95% CI)	1.00 Reference	0.95 [0.86, 1.07]
Adjusted OR (95% CI)*	1.00 Reference	0.97 [0.87, 1.09]
Asthma		
Prevalence	306/3904 (7.8%)	1357/17,888 (7.6%)
Crude OR (95% CI)	1.00 Reference	0.97 [0.85, 1.10]
Adjusted OR (95% CI)*	1.00 Reference	0.99 [0.87, 1.14]
Atopic eczema		
Prevalence	269/3904 (6.9%)	1216/17,888 (6.8%)
Crude OR (95% CI)	1.00 Reference	0.99 [0.86, 1.13]
Adjusted OR (95% CI)*	1.00 Reference	1.06 [0.93, 1.22]
Allergic rhinoconjunctivitis		
Prevalence	326/3904 (8.4%)	1322/17,888 (7.4%)
Crude OR (95% CI)	1.00 Reference	0.88 [0.77, 0.995]
Adjusted OR (95% CI)*	1.00 Reference	0.94 [0.82, 1.07]

CI = confidence interval; OR = odds ratio; RYUCHS = Ryukyus Child Health Study.

* Adjustment for sex, age, region of residence, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level.

TABLE 3.—Adjusted ORs and 95% CIs for allergic disorders according to dental caries experience among 21,792 schoolchildren with a positive or negative parental allergic history, RYUCHS, Japan.

	Adjusted OR (95% CI)*	
	Positive parental allergic history (n = 9170)	Negative parental allergic history (n = 12,622)
Wheeze	0.98 [0.85, 1.13]	0.95 [0.79, 1.14]
Asthma	0.99 [0.84, 1.17]	0.94 [0.75, 1.19]
Atopic eczema	0.99 [0.84, 1.18]	1.20 [0.95, 1.53]
Allergic rhinoconjunctivitis	0.84 [0.72, 0.99]	1.09 [0.87, 1.37]

CI = confidence interval; OR = odds ratio; RYUCHS = Ryukyus Child Health Study.

* Adjustment for sex, age, region of residence, number of siblings, smoking in the household, and paternal and maternal educational level.

Table 2 shows crude and adjusted ORs and their 95% CIs for allergic disorders in relation to the experience of dental caries. Dental caries was significantly associated with a decreased prevalence of allergic rhinoconjunctivitis. After adjusting for sex, age, region of residence, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema, or allergic rhinitis, and paternal and maternal educational level, the inverse association between dental caries and allergic rhinoconjunctivitis completely disappeared. No material relationship was observed between dental caries and the prevalence of wheeze, asthma, or atopic eczema in the multivariable model.

When study subjects were divided according to a positive or negative parental allergic history in at least one parent, an inverse association between dental caries and the prevalence of allergic rhinoconjunctivitis was apparent only in children with a positive parental allergic history (adjusted OR: 0.84 [95% CI: 0.72, 0.99]) (Table 3). However, no significant interaction was observed in the association of dental caries with the prevalence of allergic rhinoconjunctivitis between children with a positive or negative parental allergic history (p for homogeneity of OR = 0.12).

DISCUSSION

In the present cross-sectional study of Japanese children, there was no statistically significant relationship between dental caries and the prevalence of wheeze, asthma, or atopic eczema. We found that dental caries was inversely associated with the prevalence of allergic rhinoconjunctivitis only among children with a positive parental allergic history. The present findings are partially in agreement with previous findings that periodontitis or oral bacteria associated with periodontal disease had a significant relationship with decreased prevalence of allergic diseases (14, 15).

The proposed biological mechanism for the hygiene hypothesis was that the balance between T-helper type 1 (Th1) (associated with bacterial and viral infections) and Th2 (associated with allergic diseases) immune responses is pivotal (17). Dental caries is an infectious disease associated with resident microorganisms of the dental plaque (13, 18). Dental caries results from an ecological imbalance in the physiological equilibrium between tooth minerals and dental plaque (13). The mutans streptococci and *Lactobacillus* species in the dental plaque are the two groups of infectious agents most strongly associated with dental caries. The

mutans streptococci are implicated in caries initiation, and *Lactobacillus* is implicated in caries progression (18). It is not evident whether dental plaque has local and systemic effects on the immune system that could prevent allergic disease by skewing of the Th1/Th2 balance away from allergy-promoting Th2 cells toward Th1 cells. A laboratory experiment found that *S. mutans* stimulated a Th1 type of immune response while *Lactobacillus* was less polarized toward a Th1 response (19). In the human dental pulp in carious lesions, interactions between oral bacteria and the immune system are complex and the immune cell types might shift during caries progression (19).

In the current study, the inverse association between dental caries and allergic rhinoconjunctivitis was observed only among children with a positive parental allergic history, although no significant interaction was observed between children with a positive or negative parental allergic history. In our previous report using data from the RYUCHS, we found that there was an inverse association between tuberculin reactivity and the prevalence of wheeze, asthma, and atopic eczema but not allergic rhinoconjunctivitis and that the inverse associations were more pronounced in children with a negative parental allergic history than in those with a positive parental allergic history (20). These findings are inconsistent with those of the present study. Among Norwegian schoolchildren 6 to 16 years of age, recurrent respiratory tract infections during infancy were inversely associated with allergic sensitization at school age only in children without parental atopy, whereas a significant inverse association was observed between a history of otitis media in infancy and allergic sensitization at school age only among children with parental atopy (21). That study also found a significant positive association of recurrent and lower respiratory tract infections during infancy with asthma in school age only among children without parental atopy (21). That observation regarding otitis media is in partial agreement with the current results.

Several studies investigated an association between asthma and oral condition (22–25). These studies were based on the hypothesis that asthmatics may be susceptible to dental caries through a decrease of the salivary flow and plaque pH due to their medications. However, it remains unclear whether asthmatic medication is a risk factor for dental caries. A birth cohort study in New Zealand showed that there were no significant differences in caries increment between the asthmatic with anti-asthmatic medication and/or a history of wheeze and the non-asthmatic group (22). Conversely, British school children who had been previously diagnosed with asthma and were using an inhaler at the time of the study had more caries in permanent teeth than the healthy control children (23).

There are several major strengths in the present investigation. Study subjects were homogeneous with respect to age and geographical background. The large number of subjects and variables allowed us to overcome problems such as small sample size, inadequate data on potential confounders, and reduced statistical power. In addition, we used an internationally standardized and validated measurement tool (ISAAC). Data regarding dental caries were obtained from oral examinations by dentists. There are some limitations that influence the interpretation of the current results, however. Our study design was cross-sectional; therefore this study does not nec-

essarily indicate a causal relationship. The school dentists were given detail criteria for the examination, but it was uncertain whether intra-examiner and inter-examiner consistency was substantially established for this survey. Additionally, radiographic examinations were not performed in this study. Oral examinations without radiographic information are likely to underestimate the prevalence of dental caries, especially approximal and occlusal caries (26, 27). However, the misclassification of exposure with respect to disease outcome is usually random and tends to attenuate associations. In the current study, data regarding the severity of dental caries were not available. Therefore, we could not take into consideration the severity of dental caries. Although we adjusted for extensive variables, we cannot eliminate the possibility that the observed associations between dental caries and allergic diseases are a consequence of residual confounding by factors.

Of the 38,212 children at schools, 21,792 (57.0%) were included in this analysis. Regarding the 9,327 non-participants in the RYUCHS, no information on factors under study was available. It is difficult to know whether our study subjects represented a different group than those not studied in term of exposures, outcomes, or confounders under study. We compared the answers provided by 7,093 participants who were excluded because of incomplete data with answers by the 21,792 study subjects who completed all data. Compared with the 7,093 participants, the 21,792 study subjects were more likely to be male, live in Naha City, and have a personal history of atopic eczema, family members who had never smoked, fathers with a history of asthma, atopic eczema, and allergic rhinitis, mothers with a history of allergic rhinitis, and fathers and mothers with a high educational level and were less likely to be young and have dental caries and no siblings (data not shown). There was no statistically significant difference between the excluded participants and study subjects regarding the prevalence of wheeze, asthma, and allergic rhinoconjunctivitis.

Study subjects in Okinawa may differ from Japanese children in the general population and we should be cautious in generalizing the current findings. In fact, the prevalence of allergic disorders in the current study was quite different from that in the mainland of Japan. According to another cross-sectional study among Japanese adolescents in Suita City, which is in an urban area of the mainland, the prevalence values for wheeze, atopic eczema, and allergic rhinoconjunctivitis in the past 12 months based on the ISAAC criteria were 6.7%, 14.5%, and 23.9%, respectively (28).

In conclusion, there was no evidence to support the hypothesis that the presence of dental caries was protective against allergic diseases. However, a parental allergic history may affect the association between dental caries and allergic rhinoconjunctivitis. More research is needed to clarify the potential roles of dental caries in the etiology of allergic diseases.

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