Asthma medication increases dental caries among children in Taiwan: An analysis using the National Health Insurance Research Database

Fang-yi Wu, Jeng-fen Liu

Pediatric Dentistry, Taichung Veterans General Hospital, Taiwan
School of Dentistry, National Yang Ming University, Taiwan

Received 12 June 2019; Final revision received 1 August 2019
Available online 16 September 2019

KEYWORDS
Asthma; Children; Dental caries; Medication

Abstract
Background/purpose: Asthma is a common, chronic disease that causes respiratory symptoms in children. Dental caries is also a common chronic disease in the pediatric population. Therefore, the aim of the present study was to investigate the correlation between asthma medications and dental caries among children in Taiwan.

Materials and methods: The Taiwan National Health Insurance Research Database was used in this retrospective cohort study to analyze the correlation between asthma and dental caries in children. The prevalence and severity of caries were compared between children with and without asthma. The effects of different asthma medications on dental caries were also compared.

Results: A total of 4601 children with asthma and 4589 children without asthma were included in this study. The caries prevalence of children without asthma was 85.2%, and that of children with asthma was 90.0%. The prevalence of caries in children with asthma was significantly higher than that in children without asthma (P < 0.001). The caries status was categorized into mild, moderate and severe dental caries. The rate of mild dental caries was higher in children without asthma (35.1%) than in children with asthma (29.8%). The rate of severe caries was significantly higher in children with asthma (34.3%) than in those without asthma (30.7%). Also, children with asthma using bronchodilators had a higher rate of severe dental caries (39%) than in children without asthma (30.7%).

https://doi.org/10.1016/j.jds.2019.08.002
1991-7902/©2019 Association for Dental Sciences of the Republic of China. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Introduction

Asthma is a common, chronic disease that causes respiratory symptoms in children and adults. Airway inflammation and airflow limitation causes various symptoms, such as wheezing, breathlessness, chest tightness, and coughing. The treatment of asthma involves risk reduction and symptom control, and the need for asthma medication is determined according to asthma severity.\(^1\) A stepwise approach is used for asthma treatment: initially, regular low-dose inhaled corticosteroids (ICS) are administered to reduce the frequency and severity of asthma symptoms. If the symptoms worsen, short- or long-acting β₂ agonists (SABA or LABA, respectively) or short- or long-acting muscarinic receptor agonists (SAMA or LAMA, respectively) are administered in combination with ICS.

Dental caries is a common chronic disease in the pediatric population. The Taiwan National Institutes of Health (NIH) reported that from 1999 to 2004, 42% of children aged 2–11 years had dental caries in their primary teeth.\(^2\) In 2011, the prevalence of caries in children aged 5–6 years in Taiwan was approximately 79.32% (Health Promotion Administration, Ministry of Health and Welfare, Taiwan). A study of British school children reported that those with asthma had significantly greater tooth decay.\(^3\) However, a similar study of Mexican children did not identify any associations.\(^4\) Thus, the correlation of dental caries with asthma in children remains debatable. The aim of the present study was to use the National Health Insurance (NHI) database to investigate the correlation between asthma medications and dental caries among children in Taiwan. The caries prevalence and severity were compared between children with and without asthma. The effects of different asthma medications on dental caries were also compared.

Methods

Data source

The National Health Insurance (NHI) is a single-payer mandatory universal social insurance program that covers over 99% (approximately 23 million) of the Taiwanese population.\(^5\) We obtained data from the National Health Insurance Research Database (NHIRD), which comprises comprehensive administrative and claims data. The Longitudinal Health Insurance Database (LHID) 2010 was used in this retrospective cohort study to examine the correlation between asthma and dental caries in children. LHID2010 is a representative subset of NHIRD that was established by randomly selecting one million NHI beneficiaries from all NHI beneficiaries enrolled in the year 2010. Ethical approval was obtained from the Institutional Review Board of Taichung Veterans General Hospital (CE18264A).

Study population

The study population were children aged 0–9 years old with or without asthma, identified from the LHID 2010; all data for this cohort during 1996–2011 was extracted from the NHIRD.\(^6\) Children with newly diagnosed asthma were defined as those who had International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes of 493 and received the asthma treatments (i.e., ICS, LABA, SABA, LAMA, or SAMA) for at least three clinic visits or one hospital admission during 2000 and 2006 (Fig. 1). Children who developed dental caries before their first diagnosis of asthma (index date) were excluded. We selected the matched comparison group from children aged between 0 and 9 years old who did not have any history of asthma. The exclusion criteria were children diagnosed with asthma who received anti-inflammatory drugs or bronchodilator agents. Children who took anti-inflammatory drugs or bronchodilator agents were excluded because these patients might have other allergic diseases or respiratory disease. We matched children with and without asthma (approximately 1:1) for sex, age, urbanization, family income, and index date. Of the children without asthma, only those who did not have a history of dental caries prior to their index date were considered for matching. Children with asthma and children without asthma were followed from the index date until their death, or until the end of the study period (December 31, 2011).

Definition of dental caries

Children with dental caries were defined by having ICD-9-CM code of 521.0 and receiving treatment for caries during any clinic visit or hospital admission following the index date. All oral examinations and dental treatments were performed by qualified dentists. The children diagnosed with dental caries were further categorized into three groups according to the severity of their caries—(mild, moderate, and severe dental caries). Mild dental caries was defined as having dental restorations ≤5. Moderate dental caries was defined as having dental restorations 6–20. Severe dental caries was defined as having dental restorations >20 and/or having any endodontic treatment (Fig. 1).

Classification of asthma medication

Asthma medications were categorized into three groups: anti-inflammatory agents (ICS), bronchodilators (LABA,
Asthma medications increase dental caries in children

SABA, LAMA, and SAMA), and the combination of both ICS and bronchodilators. Asthma medications were further classified into three types as follows: quick-relief agents (SABA and SAMA), long-term controller medications (LABA, LAMA, and ICS), and combinations (SABA and SAMA) + (LABA, LAMA, and ICS). The caries prevalence and severity were compared between children with and without asthma. The effects of different asthma medications on dental caries were also compared.

**Statistical analysis**

SAS software version 9.4 (SAS Institute, Cary, NC, USA.) was used for all statistical analyses. A two-sample t-test (continuous variables) or chi-square test (categorical variables) was performed to compare the demographic information and the prevalence of dental caries between children with and without asthma. The chi-square test was used to investigate the influence of asthma medications on the severity of dental caries. The relative risk of dental caries associated with different asthma medications was estimated by using multivariable Cox regression analyses. The level of significance was a P-value of less than 0.05.

**Results**

A total of 4601 children with asthma and 4589 children without asthma were included in this study (Fig. 1). The caries prevalence of children without asthma (n = 4589) was 85.2%, and that of children with asthma (n = 4601) was 90.0%. The caries prevalence of children with asthma was significantly higher than that of children without asthma (P < 0.001) (Table 1). The caries status was categorized into mild, moderate and severe dental caries. The results showed that the rate of mild dental caries was higher in the children without asthma (35.1%) than in the children with...

---

**Figure 1** The selection process of the study population. ICS, inhaled corticosteroids; LABA, long-acting β2 agonists; LAMA, long-acting muscarinic antagonists; LHID, Longitudinal Health Insurance Database; SABA, short-acting β2 agonists; SAMA, short-acting muscarinic antagonists.
asthma (29.8%). Regarding severe dental caries, the rate of severe caries was higher in children with asthma (34.3%) than in those without asthma (30.7%), and the difference was significant (Table 1). Asthma medications were categorized into anti-inflammatory agents, bronchodilators, and a combination of both medications. The caries prevalence of children with asthma using anti-inflammatory agents and bronchodilators (91.3% and 92.9%) was significantly higher than that of children without asthma (Table 2). There were fewer caries free children among those with asthma using anti-inflammatory agents and bronchodilators (8.7% and 7.1%, respectively) than among children without asthma (14.8%). Regarding severe dental caries, only among children with asthma using bronchodilator had a higher rate of severe dental caries than in children without asthma (39.6% and 30.7%, respectively) (Table 2). Cox regression analysis indicated a positive correlation of dental caries with asthma medications, especially anti-inflammatory agents and bronchodilators (Table 3).

Asthma medications were further classified into quick-relief agents, long-term controllers and combinations of these two medications. Children with asthma taking quick-relief medications and long-term controllers had significantly higher prevalence of caries (92.8% and 89.3%, respectively) than children without asthma (Table 2). In these three types of medications, children with asthma taking quick-relief agents had significantly higher prevalence of caries than that in children with asthma taking the other two medications (P < 0.001). In regard to severe dental caries, only children with asthma taking quick-relief agents had a significantly higher rate of severe dental caries than children without asthma (Table 4).

### Discussion

This study analyzed NHIRD data of children to determine the correlation between dental caries and asthma. The study population included 9190 children aged 0–9 years old. This study is the first to use the NHI database to investigate the correlation between dental caries and asthmatic medication. The advantage of using the NHI database is that a large study population can be included. The results revealed a significant association between asthma and dental caries; furthermore, the use of asthmatic medication affected the prevalence and severity of dental caries.

The caries prevalence of 0–9-year-old children without asthma was 85.2%, and the caries prevalence for children with asthma was 90.0%. The children with asthma had higher caries prevalence than children without asthma, and the difference was statistically significant. These results coincide with those of Samec et al. who reported that Slovenian children with asthma had greater tooth decay.

### Table 1
Caries status of study population with and without asthma.

| Caries status          | Total (n = 9190) | Without asthma (n = 4589) | With asthma (n = 4601) | P-value* |
|------------------------|------------------|---------------------------|------------------------|----------|
| Caries free            | 1141             | 12.4%                     | 679                    | 14.8%    | 462     | 10.0%   | <0.001  |
| Dental caries          | 8049             | 87.6%                     | 3910                   | 85.2%    | 4139    | 90.0%   | <0.001  |
| Severity of dental caries |                 |                           |                        |          |         |         |         |
| Mild dental caries     | 2983             | 32.5%                     | 1612                   | 35.1%    | 1371    | 29.8%   | <0.001  |
| Moderate caries        | 3217             | 35.0%                     | 1567                   | 34.2%    | 1650    | 35.9%   | 0.09    |
| Severe caries          | 2990             | 32.5%                     | 1410                   | 30.7%    | 1580    | 34.3%   | <0.001  |
| Without severe caries  | 6200             | 67.5%                     | 3179                   | 69.3%    | 3021    | 65.7%   | <0.001  |

*Chi-square test.

### Table 2
Caries status of asthma patients according to types of medication.

| Caries status          | Without asthma (n = 4589) | Anti-inflammatorya (n = 584) | Bronchodilatorb (n = 2452) | Combinationc (n = 1565) | P-value* |
|------------------------|---------------------------|-------------------------------|----------------------------|-------------------------|----------|
| Dental caries          |                           |                               |                            |                         | <0.001   |
| Caries free            | 679                       | 14.8%                         | 51                         | 8.7%                    | 175      | 7.1%    | 236     | 15.1%   |
| Dental caries          | 3910                      | 85.2%                         | 533                        | 91.3%                   | 2277     | 92.9%   | 1329    | 84.9%   |
| Severe caries          |                           |                               |                            |                         |          |         |         |         |
| Without severe caries  | 3179                      | 69.3%                         | 399                        | 68.3%                   | 1481     | 60.4%   | 1141    | 72.9%   |
| Severe caries          | 1410                      | 30.7%                         | 185                        | 31.7%                   | 971      | 39.6%   | 424     | 27.1%   |

*Chi-square test.

a Anti-inflammatory drug: Inhaled corticosteroids (ICS).

b Bronchodilator agents: Short- or long-acting β2 agonists (SABA or LABA, respectively) or short- or long-acting muscarinic receptor agonists (SAMA or LAMA, respectively).

c Combination: ICS + (LABA, SABA, LAMA, SAMA).

d Bonferroni test (P-value < 0.05): Anti-Inflammatory vs Without asthma, Bronchodilator vs Without asthma.

e Bonferroni test (P-value < 0.05): Bronchodilator vs Without asthma.
Asthma medications increase dental caries in children

### Table 3  Relative risk (RR) for dental caries from asthma medications in logistic regression analysis.

| Asthma medication   | Dental caries | Severe dental caries |
|---------------------|---------------|----------------------|
|                     | RR  | 95% CI     | P-value* | RR  | 95% CI     | P-value* |
| Without asthma      | 1.00 |            |          | 1.00 |            |          |
| Anti-inflammatory    | 1.48 | (1.35,1.63) | <0.001   | 1.48 | (1.27,1.72) | <0.001   |
| Bronchodilators     | 1.25 | (1.19,1.32) | <0.001   | 1.38 | (1.27,1.50) | <0.001   |
| Combination         | 0.98 | (0.92,1.04) | 0.505    | 0.86 | (0.78,0.96) | 0.008    |

*Chi-square test.

### Table 4 Caries status of asthma patients according to types of medication.

| Caries status     | Without asthma (n = 4589) | Quick-relief agentsa (n = 2400) | Long-term controllersb (n = 841) | Combinationc (n = 1360) | P-value* |
|-------------------|---------------------------|---------------------------------|---------------------------------|-------------------------|----------|
| Dental cariesd    |                           |                                 |                                |                         | <0.001   |
| Caries free       | 679                       | 14.8%                           | 172                             | 7.2%                    | 90       | 10.7%   | 200     | 14.7%   |
| Dental caries     | 3910                      | 85.2%                           | 2228                            | 92.8%                   | 751      | 89.3%   | 1160    | 85.3%   |
| Severe cariesd    |                           |                                 |                                |                         |          |         |         |         |
| Without severe caries | 3179         | 69.3%                           | 1451                            | 60.5%                   | 601      | 71.5%   | 969     | 71.3%   |
| Severe caries     | 1410                      | 30.7%                           | 949                             | 39.5%                   | 240      | 28.5%   | 391     | 28.7%   |

*Chi-square test.

a Quick-relief agents: Short-acting β2 agonists (SABA), short-acting muscarinic receptor agonists (SAMA).

b Long-term controllers: Long-acting β2 agonists (LABA), long-acting muscarinic receptor agonists (LAMA), and inhaled corticosteroids (ICS).

c Combination: (SABA and SAMA) + (LABA, LAMA, and ICS).

d Bonferroni test (P-value < 0.05): Quick-relief agents vs Without asthma, Long-term controllers vs Without asthma.

e Bonferroni test (P-value < 0.05): Quick-relief agents vs Without asthma.

The study by Ryberg et al.8,9 also revealed higher caries scores (DFS) in the asthmatic group than in the control group. However, a study of Mexican children10 reported no significant differences in the prevalence of dental caries among those with (19.9%) and without (17.5%) asthma. Other studies11–14 have also described no correlations between asthma and the prevalence of dental caries in children.

The prevalence of dental caries in asthma versus the prevalence of dental caries in children without asthma was more severe in each group. Therefore, the present study further categorized dental caries into mild, moderate and severe caries. The results showed that children without asthma had a significantly higher rate of mild caries than children with asthma (35.1% vs. 29.8%). And children with asthma had a significantly higher rate of severe caries than children without asthma (34.3% vs. 30.7%). However, in regards to moderate caries there is no significant difference between asthma and non-asthma children. These demonstrated that in asthma children the caries status was more severe and the caries pattern shift from mild to moderate and severe caries compared to non-asthma children. In children without asthma, the caries status was less severe, and the caries patterns were in mild and moderate group. Therefore, there is no significant difference in moderate caries between asthma and non-asthma children. We further investigated the correlation between the severity of dental caries and the different asthma medications, and found that the severity of dental caries was related to the type of asthma medication.

The relationship between the use of asthma medications and higher caries rates among children with asthma may be due to the administration of β2-agonists. Alavaikko et al.1 indicated that the increased risk of caries in asthma may be due to β2-agonists administration, which caused a significantly lower rate of saliva secretion and higher oral microbial bacteria counts.1,15–17

In 2013, Alaki et al.18 demonstrated that the use of anti-asthma medications (β2-agonists inhalers plus corticosteroids) resulted in higher lactobacilli (LB) levels among children with asthma than that in children without asthma, but the difference was not statistically significant. Moreover, our study revealed that the children with asthma taking bronchodilator and quick-relieve agents had a higher rate of caries than the children without asthma. Both bronchodilators and quick-relieve agents contain β2-agonists. The use of asthma medications such as β2-agonists influences the saliva secretory rate.15–17 The children with asthma had a lower secretion rate of whole saliva (decreased 20%) and lower parotid saliva secretion rate (decreased 35%) compared with children without asthma (P < 0.05).19 Furthermore, children with asthma treated with β2-agonists had a significant decrease in the concentrations of total protein and amylase in the saliva, and Streptococcus mutans (SM) values were higher in these children than in children without asthma.8,19 Mazzoleni et al. analyzed the saliva of children with asthma receiving β2-agonists and reported that their saliva buffer capacity decreased and their SM and LB counts increased compared with the control group.20
In our study, the use of quick-relief agents or bronchodilators was associated with a positive correlation of severe dental caries (P < 0.001). Table 2 showed that 39.6% of children with asthma in the bronchodilator group had severe caries, which was significantly higher than that in children without asthma (30.7%). Table 4 demonstrated that 39.5% of children with asthma in the quick-relief group had severe caries, which was also significantly higher than the children without asthma (30.7%). The asthmatic patients treated with β2-adrenoceptor agonists may have reduced salivary secretory rates and increased salivary SM and LB counts, thus resulting in increasing caries susceptibility.

The asthmatic medication for children might be in the form of syrup. Syrup contains sugar or other sugar substitutes for children, which may increase the risk of dental caries. A study by Reddy et al. reported that children with asthma had high prevalence of caries and this prevalence increased with the severity of bronchial asthma. The prevalence of caries was highest in those taking medication in the form of syrup. Further research is needed to elucidate the influence of syrup-type medications for asthmatic children on the caries rate.

Nevertheless, our results indicated that even children without asthma had a prevalence of caries that was higher than 80%. Children with or without asthma should receive regular dental check-ups, fluoride applications, and reinforced oral hygiene care to decrease the prevalence of caries. Additional information, such as brushing habits, sugar consumption habits, and regular fluoride application, requires for further research and to evaluate the influence of asthma on the oral health of children. In conclusion, this study demonstrated that children receiving asthma medications had a higher prevalence of dental caries than that in children without asthma. Asthma medications also affected the severity of dental caries; children with asthma using quick-relief agents and bronchodilators had a higher rate of severe dental caries than children without asthma. These results imply that children with asthma should have more intensive preventive dental health care.

Conflicts of interest

The authors declare no conflict of interest relevant to this article.

Acknowledgments

The authors would like to thank Ching-heng Lin and Wei-szu Lin for their assistance in the statistical analysis.

References

1. Alavaikko S, Jaakkola MS, Tjaderhane L, Jaakkola JJ. Asthma and caries: a systematic review and meta-analysis. Am J Epidemiol 2011;174:631–41.
2. Tsai AI, Chen CY, Li LA, Hsiang CL, Hsu KH. Risk indicators for early childhood caries in Taiwan. Community Dent Oral Epidemiol 2006;34:437–45.
3. McDerra EJ, Pollard MA, Curzon ME. The dental status of asthmatic British school children. Pediatr Dent 1998;20:281–7.
4. Vázquez EM, Vázquez F, Barrientos MC, et al. Association between asthma and dental caries in the primary dentition of Mexican children. World J Pediatr 2011;7:344–9.
5. National Health Insurance Administration, Ministry of Health and Welfare, Taiwan. National Health Insurance 2015-2016 Annual Report. https://nhihr.nhi.gov.tw/en.
6. Chen TM. Taiwan's new national health insurance program: genesis and experience so far. Health Aff (Millwood) 2003;22:61–76.
7. Samec T, Amaechi BT, Battelino T, Krivec U, Jan J. Influence of anti-asthmatic medications on dental caries in children. Community Dent oral Epidemiol 2005;33:203–11.
8. McDerra EJ, Pollard MA, Curzon ME. The dental status of asthmatic British school children. Pediatr Dent 1998;20:281–7.
9. National Health Insurance Administration, Ministry of Health and Welfare, Taiwan. National Health Insurance 2015-2016 Annual Report. https://nhihr.nhi.gov.tw/en.
10. Zeylitzi M, Amaechi BT, Battelino T, Krivec U, Jan J. Influence of anti-asthmatic medications on dental caries in children in Slovenia. Int J Pediatr Dent 2013;23:188–96.
11. Ryberg M, Moller C, Ericson T. Effect of β2 adrenoceptor agonists on saliva proteins and dental caries in asthmatic children. J Dent Res 1987;66:1404–6.
12. Ryberg M, Moller C, Ericson T. Saliva composition and caries development in asthmatic patients treated with beta 2-adrenoceptor agonists: a 4-year follow-up study. Scand J Dent Res 1991;99:212–8.
13. Ryberg M, Moller C, Ericson T. Relationship between different types and forms of anti-asthmatic medications and dental caries in three to 12 year olds. J Dent 2016;13:238–43.
14. Tanaka K, Arakawa M, Sasaki S, Ohyama T. Dental caries and allergic disorders in Japanese children: the Ryukyu child health study. J Asthma 2008;45:795–9.
15. Ehsani S, Moin M, Meighani G, Pourhashemi SJ, Khayatpisheh H, Yarahmadi N. Oral health status in preschool asthmatic children in Iran. Iran J Allergy Asthma Immunol 2013;12:254–61.
16. Shulman JD, Taylor SE, Nunn ME. The association between asthma and dental caries in children and adolescents: a population-based case-control study. Caries Res 2001;35:240–6.
17. Meldrum AM, Thomson TW, Drummond BK, Sears MR. Is asthma a risk factor for dental caries? Finding from a cohort study. Caries Res 2001;35:235–9.
18. Alkire SM, Ashiry EA, Bakry NS, Baghlaf KK, Bagher SM. The effects of asthma and asthma medication on dental caries and salivary characteristics in children. Oral Health Prev Dent 2013;11:113–20.
19. Botelho MP, Maciel SM, Cerci Neto A, de Andrade FB, de Andrade FB. Cariogenic microorganisms and oral conditions in asthmatic children. Oral Health Prev Dent 2013;11:113–20.
20. Zenzes S, Lellini E, Cavaleri E, Angelova VA, Ferro R, Fochezato CS. Dental caries with asthma undergoing treatment with β2-agonists. Eur J Pediatr Dent 2008;9:132–8.
21. Reddy DK, Hegde AM, Munshi AK. Dental caries status of children with bronchial asthma. J Clin Pediatr Dent 2003;27:293–6.