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Original Article

## Impact of periodontal treatment on hospitalization for adverse respiratory events in asthmatic adults: A propensity-matched cohort study

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### ABSTRACT

**Background:** Periodontal disease is prevalent in asthmatics, but it is unclear whether periodontal treatment plays a role in adverse respiratory events in these patients. We evaluated risk of hospitalization for adverse respiratory events (acute exacerbation, pneumonia, and acute respiratory failure) and mortality in asthmatic adults with and without periodontal treatment.

**Methods:** We used National Health Insurance (NHI) claims data of Taiwan to identify 4771 asthmatic adults with periodontal disease who underwent periodontal treatment during 2000–2006. The control group consisted of asthmatic adults without periodontal disease at a 1:1 ratio matched by the propensity score. Both groups were followed up for 5 years to estimate the risk of hospitalization for adverse respiratory events and mortality.

**Results:** Compared with controls, the periodontal treatment group had lower overall incidence of hospitalization for adverse respiratory events [5.41 vs. 6.07 per 100 person-years, 95% confidence interval (CI) = 0.78–0.92] and intensive care unit admissions (1.14 vs. 1.25 per 100 person-years, 95% CI = 0.79–0.99). In addition, the all-cause mortality rate was significantly lower in the periodontal treatment group than in the control group during the follow-up period (1.86 vs. 2.79 per 100 person-years, 95% CI = 0.59–0.71).

**Conclusion:** Asthmatic adults who underwent periodontal treatment were at lower risk of hospitalization for adverse respiratory events and mortality than those without periodontal disease. Asthmatic adults should adopt more precautionary oral hygiene and ensure that they undergo regular periodontal health checkups.

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### 1. Introduction

Asthma is a chronic airway inflammatory disease that imposes a substantial burden on patients and families worldwide. Patients suffer from asthma may experience shortness of breath, chronic cough, and chest tightness. Exacerbations of an uncontrolled asthma can be fatal. The optimized medications and timely intervention on modifiable

comorbidities can reduce asthma exacerbations and improve the quality of life [1].

Periodontal disease is also an inflammatory disorder and involves tissues surrounding and supporting the teeth, such as gingivitis and periodontitis [2]. Periodontal disease is usually caused by a bacterial biofilm on the teeth, but other genetic and environmental factors are also contributory [3]. The associations between asthma and oral conditions such as dental caries, dental erosion, and periodontal disease have been investigated, and some studies have focused on asthma and periodontal disease [4–7].

Both mouth and teeth are reservoirs for potential respiratory pathogens, and the aspiration of virulent pathogen-contaminated saliva may cause respiratory infections [8]. >700 different bacterial species and other microorganisms may develop on the dental plaque in people with poor oral hygiene [9]. Therefore, evidence indicates that

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periodontal disease is strongly associated with respiratory infections, including community-acquired or nosocomial pneumonia [10,11]. In addition, some studies have reported that periodontal treatment can reduce the risk of pneumonia in certain populations [12]. However, the effect of periodontal treatment on the risk of adverse respiratory events in patients with asthma remains largely unknown.

The National Health Insurance Research Database (NHIRD) in Taiwan is a nationwide database, containing claims cohort data of 23 million people. These reliable data have been used in various studies, including asthma or periodontal disease and its treatment [13–16]. We hypothesized that periodontal treatment could be beneficial for reducing adverse respiratory events in asthmatics. The aim of the present study was to investigate periodontal treatment and the subsequent risk of adverse respiratory events, including acute exacerbation, pneumonia, and acute respiratory failure (ARF) in asthmatic adults. We also compared the mortality between asthmatic patients with and without periodontal disease.

## 2. Materials and methods

### 2.1. Data source

Taiwan launched the National Health Insurance (NHI) program in March 1995, and over 99.5% of people in Taiwan have enrolled in this program [17]. In this study, we used one of NHIRDs, the Longitudinal Health Insurance Database 2000 (LHID2000), which contains longitudinal medical data of one million insurance beneficiaries randomly selected from all beneficiaries file in 2000. The National Health Research Institutes (NHRI) managed and updated the claims data. All personal identifications were encrypted to protect their privacy. Diseases were recorded according to the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)*. This study was evaluated and approved by the Research Ethics Committee of China Medical University and Hospital (CMUH-104-REC2-115).

### 2.2. Sampled participants

From the claims data from 2000 to 2006, we identified adult patients with a new diagnosis of asthma (*ICD-9-CM* code 493) and without a previous history of periodontal disease (*ICD-9-CM* code 523) for possible study participants. We identified only inpatients hospitalized for asthma and outpatients receiving at least 2 prescriptions for asthma in 1 year as our study population to assure the validity and accuracy of diagnoses. The prescriptions for asthma included short-acting  $\beta_2$  agonist (SABA), systemic corticosteroid, inhaled corticosteroid (ICS), ICS plus long-acting  $\beta_2$  agonist (ICS + LABA), aminophylline/theophylline, leukotriene receptor antagonist (montelukast). Thus, those who were newly diagnosed with periodontal disease and underwent periodontal treatment {included subgingival curettage [scaling (91004C) and root planning (91006C, 91007C, 91008C)] and periodontal flap surgery (91009B, 91010B)} were included in the periodontal treatment group (case group) [12]. The date of the first periodontal treatment was defined as the index date. The control group comprised individuals selected from the remaining asthmatics without periodontal disease during the whole study period. The periodontal treatment group and the control group were established with the allocation ratio of 1:1, matched by the propensity score. The propensity score was calculated using a logistic regression to estimate the probability of the treatment assignment according to baseline variables, including age, sex, index date, monthly income, urbanization level, comorbidities of hypertension (*ICD-9-CM* codes 401–405) [18], heart failure (*ICD-9-CM* code 428), diabetes (*ICD-9-CM* code 250), allergic diseases [allergic rhinitis (*ICD-9-CM* code 477), chronic sinusitis (*ICD-9-CM* code 473), and atopic dermatitis (*ICD-9-CM* code 691)], chronic obstructive pulmonary disease (COPD) (*ICD-9-CM* codes 496) [19], obstructive sleep apnea syndrome (OSAS) (*ICD-9-CM* codes 327.23, 780.51, 780.53, and 780.57), mental disorders

(*ICD-9-CM* codes 290–319) [20], gastroesophageal reflux disease (GERD) (*ICD-9-CM* codes 530.11 and 530.81) and obesity (*ICD-9-CM* code 278), and level of asthma therapy [maintenance oral corticosteroid (OCS), ICS + LABA, ICS only, and others].

### 2.3. Outcome measurements

The duration of follow-up (person-years) was measured for all individuals from the index date for up to 5 years or until the patient was censored because of death or withdrawal from the insurance system within 5 years. The outcomes of interest in this study were determined according to the number of adverse respiratory events, that is, acute asthma exacerbation, pneumonia (*ICD-9-CM* code 486), and ARF (*ICD-9-CM* code 518.81) from hospitalization records.

### 2.4. Statistical analysis

The baseline characteristics were compared in the case group and in the control group. The categorical variables were analyzed using the Chi-square test, and the continuous variables were analyzed with the Student's *t*-test. Incidence rates of outcomes were calculated by covariate during the 5-year follow-up. Univariate and multivariate Poisson regression models were employed to estimate the incidence rate ratios (IRRs) and 95% confidence intervals (CIs) of developing adverse respiratory events for the case group and the control group. The multivariate models were adjusted for age, sex, monthly income, urbanization level, comorbidities, and level of asthma therapy. We further compared mortality risk between the two groups. Data processing and statistical analyses were performed using SAS Version 9.4 (SAS Institute, Inc., Cary, NC, USA). A two-tailed *p* value < 0.05 was considered statistically significant.

## 3. Results

The present study included 4771 asthmatic adults with periodontal treatment and 4771 asthmatic adults without periodontal disease, who were matched by their propensity scores (Table 1). The means  $\pm$  standard deviations (SD) of age in the case group and the control group were  $61.9 \pm 16.6$  and  $62.2 \pm 16.6$  years, respectively. There were no significant differences in the distributions of age, sex, income, urbanization, comorbidities, and level of asthma therapy between the case group and the control group.

During the 5-year follow-up, a lower overall incidence of hospitalization for adverse respiratory events was observed in the case group than in the control group (5.41 vs. 6.07, per 100 person-years), with an adjusted IRR of 0.84 (95% CI = 0.78–0.92; Table 2). Among these events, the case group had a significantly lower incidence of acute exacerbation (1.06 vs. 1.13 per 100 person-years), pneumonia (1.96 vs. 2.64 per 100 person-years), and ARF (1.74 vs. 2.92 per 100 person-years), with adjusted IRRs of 0.92 (95% CI = 0.83–1.03), 0.72 (95% CI = 0.66–0.79) and 0.58 (95% CI = 0.53–0.64), respectively, compared to the control group. In addition, the incidence of intensive care unit (ICU) admission for these events was also significantly lower in the case group than in the control group (1.14 vs. 1.25 per 100 person-years), with an adjusted IRR of 0.88 (95% CI, 0.79–0.99).

The periodontal therapy had beneficial effects on hospitalization and was significant in the elderly, in men, in middle income population, and greater in residents living in non-urbanized areas (Table 3). The hospitalization incidence increased with presence of maintenance OCS and COPD, but the therapy effectiveness was significant for asthmatics receiving the basic treatments and ICS alone, for those without maintenance OCS, and for those comorbid with COPD. Furthermore, the all-cause mortality rate was significantly lower in asthmatic adults with periodontal treatment than those without periodontal disease (1.86 vs. 2.79 per 100 person-years), with an adjusted IRR of 0.65 (95% CI = 0.59–0.71) for the periodontal group (Table 4).

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