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The association between bronchial asthma and periodontitis: a case-control study in Jordan

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Abstract

Objective: Our aim is to study the association between bronchial asthma (BA) and periodontitis in northern Jordan.

Methods: A case-control study of 260 subjects; 130 with BA and 130 without BA (controls) were recruited from pulmonary clinics at a university hospital in northern Jordan. BA cases were physician-diagnosed and subjects had been prescribed anti-asthma medications for ≥ 12 months. Periodontitis was defined as the presence of ≥ 4 teeth with ≥ 1 site with probing pocket depth (PPD) ≥ 4 mm and clinical attachment level (CAL) ≥ 3 mm.

Results: Mean age of participants was 45.3 years (range, 18-65) and 58.1% were females. Patients with BA had lower education and tended to live in rural areas. Periodontitis was present in 52 (40.0%) patients with BA and 26 (20.0%) in the control group, $p < 0.005$. Binary logistic regression indicated patients with BA were more likely to have periodontitis than controls [adjusted odd ratio (OR) = 2.91, 95% CI (1.39-6.11), $p = 0.005$]. Patients with BA had higher percentage of sites with: PPD ≥ 3 , CAL ≥ 3 , and CAL ≥ 4 than controls, $p < 0.05$. The risk of periodontitis [OR = 5.27, 95% CI (1.59-17.51)] and CAL ≥ 3 were higher in patients on oral corticosteroids compared to inhaled corticosteroids, $p < 0.05$.

Conclusions: Adult Jordanians with bronchial asthma are at higher risk of periodontitis. The risk differs by the type of treatment, being highest with oral corticosteroid use, and lowest with inhaled corticosteroids. Large and longitudinal studies are needed to better understand this significant association.

Introduction

Bronchial asthma (BA) is a respiratory disease characterized by chronic airway inflammation and expiratory airflow limitation¹. The prevalence of asthma has been increasing across all ages, gender, and racial groups since the 1960s with more than 330 million people affected worldwide². Periodontal diseases comprise a wide range of inflammatory conditions that affect the supporting structures of the teeth³. Chronic periodontitis is primarily an adult disease with accumulating evidence of association with systemic diseases, including diabetes, adverse pregnancy outcomes, chronic obstructive pulmonary disease, pneumonia, chronic kidney disease, rheumatoid arthritis, cognitive impairment, obesity, metabolic syndrome, and cancer^{4,5,6}.

Oral health, including periodontal disease is a concern in patients with BA. The association between BA and periodontal disease may involve either pathological activation of the immune and inflammatory process, side effects of anti-asthma medications, or an interaction between them^{7,8,9}. The effect of inhaled medications on oral health is the subject of debate and there is no conclusive statement on the role of anti-asthma inhalers in periodontal disease^{10,11}. Population-based and case-control studies have shown that BA is associated with periodontitis^{12,13,14,15,16,17,18}. A recent meta-analysis by Moraschini et al. strongly suggests a positive association between BA and periodontal disease¹⁹. However, studies were done in different populations and used various definitions of BA and periodontal disease.

Periodontal disease appears to be common in northern Jordan; 70% had gingivitis and 5.5% had chronic periodontitis²⁰. One study addressed the prevalence of BA in Jordan and showed that almost one in ten Jordanian children have BA²¹. The association between these two common diseases has not been well addressed in the eastern Mediterranean region. Also, few studies in the adult population used well-defined criteria of periodontitis. The purpose of this study was to describe the association between periodontitis and both BA and anti-asthma medications in pulmonary specialty clinics in northern Jordan.

Methods:

Study sample

A case-control study was conducted over a 6-month period to examine the association between BA and periodontitis. Patients with BA were recruited from consecutive adult patients attending pulmonary specialty outpatient clinics at a university hospital in northern Jordan. The hospital is a 600-bed referral hospital for a population of 2.8 million (one third of Jordan's population). BA cases were diagnosed by a

pulmonary consultant and had been on anti-asthma medications for at least 12 months. Subjects without any respiratory or chronic medical illnesses (controls) were recruited using a flyer in the pulmonary clinic inviting non-patient subjects with no known chronic or respiratory illnesses to participate in the study.

Patients and controls were excluded if they had: other respiratory illness (BA patients) or any respiratory illness (controls), systemic disease that might affect the severity of periodontal disease such as immune-deficiency and diabetes mellitus, complete edentulism, disease requiring prophylactic antibiotic, or a current asthma exacerbation (BA patients). Pregnant women, and patients under any periodontal or orthodontic treatment were also excluded.

Recruited subjects were invited to complete the self-administered periodontal questionnaire and then underwent periodontal clinical examination. The questionnaire was specifically developed for this study and included sociodemographic items: age, gender, occupation, monthly income (low vs high), highest level of education (elementary school, high school, university degree), residency (urban vs rural), and smoking status (smoker vs non-smoker). It also included questions related to dental health: When was your last dental visit? Why was your last dental visit? Do you use dental aids? Do you regularly use mouth wash? Additionally, there were questions related to BA: How long have you had BA? What are your regular anti-asthma medications? Have you taken oral corticosteroids in the last 6 months? Does your dentist know that you have BA? Did you tell your dentist that you are taking anti-asthma medications? Do you believe that your oral health is related to having BA or taking anti-asthma medications? Lastly there were questions related to the exclusion criteria: Do you have a chronic respiratory illness? Do you have any chronic medical illness?

The list of anti-asthma medications for subjects with BA were also collected from their medical and pharmacy records and divided into three groups. Group 1: regular oral corticosteroids (OCS) or at least two short courses of OCS in the preceding 6 months; group 2: regular inhaled corticosteroids (ICS) with or without long-acting beta-2-agonists; and group 3: as-needed inhaled bronchodilators only [short-acting beta-2-agonists (SABA)].

Periodontal Examination

All participants meeting the inclusion and exclusion criteria (BA=130) and (controls=130) were examined by the same examiner, who was blinded to the study groups. The oral hygiene and the periodontal status of all teeth, excluding third molars, were assessed using the plaque index of Silness & Loe and the gingival index of Loe & Silness^{22,23}. Sterile dental mirrors and explorers were used to assess plaque accumulation and gingival status, and standardized periodontal probes were used to measure probing pocket depth and clinical attachment loss. The parameters were measured at six sites (mesiofacial, midfacial, distofacial, mesiolingual, midlingual and distolingual) per tooth using standardized Michigan 0 periodontal probes with Williams's markings (Diatech, Switzerland). The means of pocket index (PI), gingival index (GI), plaque probing depth (PPD), and clinical attachment level (CAL) over all sites as well as percentages of sites with CAL of ≥ 3 , CAL ≥ 4 mm, PPD ≥ 3 mm, and PPD ≥ 4 mm were calculated for each participant. Periodontitis was defined as the presence of ≥ 4 teeth with ≥ 1 site with PPD ≥ 4 mm and CAL ≥ 3 mm²⁴. The American Academy of Periodontology task force identified a general guide for the "severity" of periodontitis based on CAL, and the "extent" of the disease by the percentage of affected sites using PPD and CAL measurements from all six sites per tooth²⁵.

Statistical Analyses:

The Statistical Package for Social Sciences software (SPSS Inc., version 23) was used for data processing and data analysis. A p-value of <0.05 was considered statistically significant for all performed analyses. Characteristics of subjects' variables were described using frequency distribution for categorical variables and mean and standard deviation for continuous variables. Tests of significance between groups were carried out using Chi-square test for categorical variables (socio-demographics) and student t-test for continuous variables (age). Analysis of covariance (ANCOVA) adjusted for age, gender, income, highest education, residency, and smoking was used to study the association between study groups or anti-asthma medications groups, and the mean for the periodontal parameter: PI, GI, PPD, CAL, GR, number of missing teeth, and bleeding on probing and the percentage of surfaces with: $PPD \geq 3$, $PPD \geq 4$, $PPD \geq 5$, $CAL \geq 3$, $CAL \geq 4$ and $CAL \geq 5$. Binary logistic regression was conducted to determine the association between bronchial asthma or anti-asthma medications and periodontitis after adjusting for confounders (gender, age, plaque index, highest education, income, residency, number of missing teeth and smoking). Unadjusted and adjusted odds ratios (ORs) and their 95% confidence interval (CI) were calculated.

This study was conducted in full accordance with the World Medical Association Declaration of Helsinki. The study was approved by the local institutional review board.

Results

Participant's Characteristics

A total of 260 participants (BA = 130) and (controls = 130) were included in the analysis with a mean age of 45.3 years (range, 18-65 years), 58.1% were females. Patients with BA had lower education ($p < 0.005$)

and tended to live in rural areas ($p=0.032$). The majority of patients with BA (88.5%) did not believe that BA or anti-asthma medications affect oral health, and 70.8% did not report having BA to their dentist. Table 1 shows the socio-demographic characteristics of participants according to study groups and periodontitis status.

Periodontitis and Bronchial Asthma

According to the study definition, 78 (30.0%) of all study subjects had periodontitis. Periodontitis was present in 52 (40.0%) patients with BA and 26 (20.0%) of controls, $p<0.005$. Table 2 shows the binary logistic regression models with unadjusted and adjusted odds ratios. Patients with BA were more likely to have periodontitis than the controls (adjusted OR = 2.91, 95% CI (1.39-6.11), $p=0.005$). Also, the risk of periodontitis was significantly increased in males (adjusted OR = 4.54) and with increasing age (OR = 1.07), $p < 0.005$.

Table 3 shows ANCOVA analysis comparing periodontal parameters (severity and extent of periodontal disease) between patients with BA and controls. Mean CAL score, mean gingival recession (GR) and number of missing teeth were higher in patients with BA than controls, $p < 0.01$. The percentage of sites with PPD ≥ 3 mm, CAL ≥ 3 , CAL ≥ 4 , and bleeding on probing were higher in patients with BA compared with controls, $p<0.01$.

Periodontitis and Anti-asthma medications

Approximately half of patients with BA (44.6%) received regular ICS and 28.5% were on regular or intermittent OCS, while 26.9% were on inhaled bronchodilators (SABA). Periodontitis was more common in patients receiving OCS (56.8%) compared to those receiving ICS (24.1%), $p=0.001$, but there was no

significant difference between the ICS group and the SABA group (48.6%), $p=0.487$. Since SABA was used as a rescue medication with OCS or ICS, we compared between patients who received only OCS ($n=6$) and only ICS ($n=15$). None of the ICS group and 3 out of 6 of the OCS group had periodontitis.

In binary logistic regression (Table 2), patients with BA who received OCS were more likely to have periodontitis compared with those who received ICS [adjusted OR = 5.27, 95% CI (1.59-17.51), $p<0.005$].

Table 4 shows details of ANCOVA analysis comparing various periodontal parameters among the groups of anti-asthma medications. Mean GR was the highest in the OCS group ($p=0.001$), but there were no significant differences among the groups for PD, CAL, number of missing teeth, and BOP. The “extent” of periodontal disease, using percentage of sites with $CAL \geq 3$, was the highest in the OCS group, $p=0.021$, but there were no significant differences in the percentage of sites with $CAL \geq 4$, $CAL \geq 5$, $PPD \geq 3$ and $PPD \geq 4$.

Discussion

This study used a well-defined criteria for the diagnosis of periodontitis and included detailed measurement of periodontal parameters. Cases of BA were identified by a respiratory consultant and were on medications for at least 12 months. Our results showed a significant positive association between BA and periodontitis. Patients with BA were three times more likely to have periodontitis than controls, and “extent” and “severity” of periodontal disease were significantly higher in patients with BA. Moreover, patients on OCS were more likely to have periodontitis compared with those on ICS.

Our results are consistent with previous studies that showed a positive association between BA and periodontal disease in the adult population. Two large population-based studies addressed the association between BA and periodontitis. The first was a large cross-sectional study from Korea that

used Community Periodontal Index to define periodontitis cases while BA was self-reported¹⁸. The main results showed that asthmatics are five times more likely to have periodontitis than controls in the general population. A population-based study from Taiwan studied the risk of periodontal diseases in patients with BA. The overall incidence of periodontal disease was 1.18 times higher in the asthmatic cohort, and the risk was even higher in asthmatics with frequent emergency visits¹⁷. This wide range of risk of association emphasizes the importance of the studied population, study design and case definitions when interpreting prevalence studies²⁴. Similarly, case control studies in adults with BA showed a positive association with periodontal disease. Gomes-Filho et al. reported that the risk of periodontitis in patients with severe bronchial asthma increased by five times¹⁵. Severe asthma was identified according to the Global Initiative for Asthma guidelines and CAL, PD and BOP measurements were used to define periodontitis^{1,15}. Two other studies from India showed that patients with BA had higher modified gingival index and higher CAL^{13,16}. Yaghoobee et al. reported several measurements in patients with BA and controls in Iran, where asthmatics had higher PI, GI, PBI, and PDI¹². On the other hand, a large study in adolescents in the United States concluded that there was no association between BA and periodontal health in the adolescent population²⁶. A study from Germany evaluated the association between periodontitis and respiratory allergies, including BA, and showed a weak but inverse relationship between respiratory allergies including BA and periodontitis²⁷.

A recent systematic review and meta-analysis of the association between BA and periodontal disease showed that patients with BA have higher gingival bleeding, PI, and gingival index¹⁹. The authors concluded that although cumulative data strongly suggests an association between the two diseases, there were important differences between the reviewed studies, with a wide range of case definitions of BA, and the use of different parameters to define periodontal disease. Their findings emphasized the need for more longitudinal studies to better describe this association¹⁹. Compared to studies in the

systemic review, the strengths of our study were the case-control design, inclusion of only pulmonary specialist-diagnosed BA cases, and utilization of periodontal parameters adopted by the American Academy of Periodontology to diagnose periodontitis and define its “severity” and “extent”²⁵.

This study also addressed the role of anti-asthma medications and showed that treatment with OCS is associated with increased risk and “extent” of periodontitis. Similarly, previous studies showed that patients with moderate to severe BA had higher CAL than patients with mild BA¹⁵. Also, children with BA who were taking bronchodilators had higher risk of periodontal disease than those on ICS²⁸. The severity of BA and regular use of inhaled medications appear to alter salivary flow and characteristics in children with BA²⁹. An indirect factor could be the dryness of the mouth caused by some of the medications³⁰. Ryberg et al. observed that the secretion rates of whole and parotid saliva decreased by 26% and 36% in asthmatics on medication when compared to the non-asthmatic control group³¹.

Other studies have indicated that ICS is associated with increased levels of gingivitis and decrease in bone mineral density^{32,33}. Hanania et al. in their study showed that regular use of conventional doses of ICS by patients with asthma can suppress the adrenal function and decrease bone density in a dose-related fashion³³. Systemic bone loss caused by these drugs, especially when high doses are used for a long time, may have an impact on the onset and progression of periodontal disease³⁴. Individuals taking ICS, regardless of having BA, had a decreased salivary total IgA level¹⁰. It has been postulated that mouth breathing in patients with bronchial asthma leads to dehydration of alveolar mucosa which contributes to development of periodontitis⁸.

The present study had a few limitations. Both BA subjects and controls were convenience samples recruited from a tertiary hospital in northern Jordan with inherent selection bias, consequently limiting the applicability of our findings to the general population in Jordan. Nonetheless knowledge of this

association is valuable in guiding the care of patients attending pulmonary specialty clinic. Controls were a random sample of hospital non-patient visitors that were not age and gender matched. However, they did not have any chronic respiratory or medical illness, and we adjusted for their demographic differences in the analysis.

This study described the association between periodontitis and major groups of anti-asthma medications, but it was not designed to account for the differences in delivery devices and inhaled molecules. There is a growing number of inhaler devices used to deliver an ever-increasing list of inhaled medications with variable drug delivery and deposition in the oropharyngeal area³⁵. Most guidelines consider combination inhalers of CS and long-acting bronchodilators the standard therapy for most cases of BA^{1,36}. Further complicating the issue, most dry powder inhalers are sugar-based while others like metered-dose inhalers are not³⁷. Building on the observations in this study and previous reports, future studies are needed on the effects various inhaler devices, inhaled medications, and carrier molecule on periodontal health.

Conclusions: Adult Jordanians with bronchial asthma are at higher risk of periodontitis. The risk differs by the type of asthma treatment, being highest with oral corticosteroids and lowest with inhaled corticosteroids. Large and longitudinal studies are needed to better understand this significant association. Meanwhile, health care providers of patients with bronchial asthma are encouraged to discuss this association with their patients and recommend regular periodontal health checks.

Conflicts of interest and source of funding statement

Authors declare no conflicts of interest.

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Table 1: Socio-demographic characteristics of study participants (bronchial asthma and controls) and according periodontal status.

Variable	Study Groups			Periodontitis		
	Bronchial Asthma n=130	Controls n=130	p-value	Yes n=78	No n=182	p-value
Age (years) m±sd	46.43±12.24	44.18±11.85	0.134 ^a	52.87±9.10	42.07±11.76	<0.005 ^a
Gender						
Male	56 (43.1)	53 (40.8)	0.706 ^b	55 (70.5)	54 (29.7)	< 0.005 ^b
Female	74 (56.9)	77 (59.2)		23 (29.5)	128 (70.3)	
Income/month						
≤ 250	43 (33.1)	40 (30.8)	0.690 ^b	30 (38.5)	53 (29.1)	0.139 ^b
> 250	87 (66.9)	90 (69.2)		48 (61.5)	129 (70.9)	
Highest Education						
Elementary school	44 (33.9)	23 (17.8)	< 0.005 ^b	27 (34.6)	40 (22.1)	0.006 ^b
High school	57 (43.8)	58 (45.0)		38 (48.7)	77 (42.6)	
University degree	29 (22.3)	48 (37.2)		13 (16.7)	64 (35.4)	
Residency						
Urban	116 (89.2)	125 (96.2)	0.032 ^b	69 (88.5)	172 (94.5)	0.086 ^b
Rural	14 (10.8)	5 (3.8)		9 (11.5)	10 (5.5)	

Smoking status							
Smoker	31 (24.0)	44 (34.2)	0.068 ^b		22 (28.6)	53 (29.4)	0.888 ^b
Non-smoker	98 (76.0)	84 (65.6)			55 (71.4)	127 (70.6)	

^a Student t-test, ^b chi-square test

Table 2. Results of unadjusted and adjusted binary logistic regression models of factors associated with periodontitis.

Variable	Study Groups n=260				Anti-asthma Medications Groups n=130			
	Unadjusted Model		Adjusted Model ^a		Unadjusted Model		Adjusted Model ^a	
	OR (95% C.I.)	p value	OR (95% C.I.)	p value	OR (95% C.I.)	p value	OR (95% C.I.)	p value
Bronchial asthma vs controls	2.67 (1.53-4.64)	<0.005	2.91 (1.35-6.11)	0.005	-	-	-	-
OCS vs ICS ^b	-	-	-	-	4.13 (1.70-10.00)	0.002	5.27 (1.59-17.51)	0.007
Male gender	5.67 (3.17-10.14)	<0.005	4.54 (2.13-9.68)	<0.005	3.13 (1.51-6.49)	0.002	6.28 (1.77-22.33)	0.005
Age (years)	1.10 (1.07-1.14)	<0.005	1.07 (1.03-1.11)	<0.005	1.06 (1.02-1.09)	0.001	1.03 (0.97-1.09)	0.332
Plaque index	3.81 (2.37-6.11)	<0.005	2.06 (1.18-3.58)	0.011	2.25 (1.31-3.85)	0.003	1.33 (0.62-2.85)	0.469
Education - High school	0.731 (0.39-1.36)	0.325	1.07 (0.38-3.05)	0.895	1.13 (0.43-2.96)	0.799	0.45 (0.1-2.10)	0.306
Education - University degree	0.30 (0.14-0.65)	<0.005	0.87 (0.35-2.20)	0.769	1.11 (0.44-2.77)	0.828	0.70 (0.18-2.77)	0.612
Low Income	1.52 (0.87-2.66)	0.14	1.52 (0.71-3.27)	0.285	1.30 (0.62-2.72)	0.494	1.33 (0.40-4.33)	0.646
Rural Residency	2.24 (0.87-5.76)	0.093	0.38 (0.10-1.38)	0.177	3.06 (0.96-9.71)	0.058	3.03 (0.58-15.82)	0.188
Number of missing teeth	1.15 (1.09-1.22)	<0.005	1.08 (1.00-1.15)	0.043	1.15 (1.07-1.23)	<0.001	1.11 (1.00-1.24)	0.062

Smoking	1.04 (0.58-1.88)	0.888	1.61 (0.75-3.47)	0.224	0.90 (0.39-2.06)	0.803	0.50 (0.13-1.95)	0.316
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^a Adjusted for all variables in the model

^b OCS: oral corticosteroids, ICS: inhaled corticosteroids

Table 3: Analysis of covariance (ANCOVA) of the mean (SD) scores of periodontal parameters between bronchial asthma and controls.

Periodontal Parameters	Bronchial Asthma n=130	Controls n=130	p-value ^a
Plaque Index	1.66 (0.73)	1.57 (0.66)	0.301
Gingival Index	1.66 (0.54)	1.58 (0.53)	0.262
Plaque Probing Depth (PPD)	2.06 (0.23)	2.02 (0.08)	0.195
Clinical Attachment Level (CAL)	2.35 (0.60)	2.14 (0.27)	0.011
Gingival Recession	0.31 (0.51)	0.12 (0.24)	0.007
Number of missing teeth	5.39 (6.11)	2.98 (3.80)	<0.001
Bleeding on probing	21.2 (15.00)	19.9 (13.60)	0.010
Percentage of sites with			
PPD ≥ 3	5.05 (14.52)	0.62 (2.56)	0.012

PPD $\geq$ 4	1.18 (6.96)	0.07 (0.55)	0.332
PPD $\geq$ 5	0.17 (1.91)	0.00 (0.00)	0.596
CAL $\geq$ 3	21.9 (31.60)	10.1(18.4)	0.009
CAL $\geq$ 4	9.61 (20.10)	2.79 (7.70)	0.014
CAL $\geq$ 5	2.98 (10.56)	0.70 (3.33)	0.213

^aAdjusted for age, gender, income, highest education, residency and smoking.

Table 4. Analysis of covariate (ANCOVA) of the mean (SD) scores of periodontal parameters among different groups of anti-asthma medications.

Periodontal parameters	Group of Anti-Asthma Medications			P-value ^a
	Oral Corticosteroids n=37	Inhaled Corticosteroids n=58	Bronchodilators (SABA) ^b n=35	
Probing depth (PD)	2.05 (0.114)	2.04 (0.97)	2.12 (0.40)	0.337
Clinical attachment level (CAL)	2.53 (0.68)	2.21 (0.46)	2.40 (0.69)	0.071
Gingival recession	0.53 (0.65)	0.18 (0.40)	0.28 (0.40)	0.001
Missing teeth	7.10 (6.83)	3.98 (5.48)	5.91 (5.90)	0.122
Bleeding on probing	24.4 (20.70)	17.8 (18.3)	23.4 (21.40)	0.188
Percentage of sites with:				
PD $\geq$ 3	4.74 (10.0)	3.56 (9.51)	7.85 (23.0)	0.646
PD $\geq$ 4	0.85 (3.51)	0.06 (0.49)	3.40 (12.8)	0.186
PD $\geq$ 5	0.00 (0.00)	0.00 (0.00)	0.62 (3.67)	0.153

CAL $\geq$ 3	32.7 (37.40)	14.4 (25.70)	22.9 (31.40)	0.021
CA $\geq$ 4	15.1 (23.00)	5.27 (15.90)	11.00 (21.80)	0.097
CAL $\geq$ 5	4.89 (13.00)	1.60 (7.71)	3.23 (11.70)	0.474

^a Adjusted for age, gender, income, highest education, residency and smoking

^b SABA: Short acting beta-2 agonist

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