RESEARCH ARTICLE

Impact of Secretory Immunoglobulin A Level on Dental Caries Experience in Asthmatic Children

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Abstract

Objectives: To assess the association between different factors in saliva and dental caries experience in children with bronchial asthma.

Materials and methods: A total of 60 asthmatic children and 60 healthy controls of both genders with age ranging from 4- to 12-year-old. The asthmatics were grouped according to disease severity into mild, moderate, or severe asthma. All the children were clinically examined to assess their dental caries experience (deft/DMFT), and stimulated saliva samples were collected to measure the saliva pH, flow rate, ά-amylase, and secretory immunoglobulin A (sIgA)-level changes. The data were statistically analyzed using the SPSS program (v. 23) to test for significance at $p \leq 0.05$.

Results: Asthmatic children presented significantly higher deft mean value (6.77 ± 1.69), as well as significantly reduced stimulated saliva flow (0.82 ± 0.2) and sIgA (29.42 ± 6.31) when compared to healthy control. The sIgA of asthmatics showed statistically significant negative correlation with deft and DMFT. Severe asthmatics presented significantly the lowest sIgA mean level (23.61 ± 5.33) and the most reduced saliva flow rate (0.64 ± 0.20).

Conclusion: The reduction in saliva flow rate and secretory immunoglobulin A render asthmatic children more prone to increased dental caries progression mainly of primary dentition.

Keywords: Asthma, Children, Dental caries, Saliva, Secretory immunoglobulin A.

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Introduction

Bronchial asthma is one of the most common chronic diseases that affect variable individuals particularly children and characterized by repeated raids of chest wheeze and breathlessness owing to hyperresponsiveness and pathological narrowing of the respiratory air-passages. Chronic asthma accounts for one of the topmost 10 chronic-disability-adjusted life conditions in children.[1] Several studies have demonstrated a considerable increase in the prevalence of wheeze and asthma in children.[2,3] The Global Asthma Network reported increased asthma symptoms and severity particularly in low- to middle-income countries.[4]

Early manifestation of bronchial asthma at the first year of life can cause dento-facial changes. Therefore, the prompt diagnostic of the illness, as well as the establishment of a proper therapy could improve the symptoms and chronic complications of asthma and also reduce its adverse impact on craniofacial development.[5]

The relationship between persistent bronchial asthma and dental caries incidence has been studied widely but with controversy results. However, a recent meta-analysis investigation has reported that caries incidence found almost doubled in asthmatic subjects both for primary and permanent dentition compared to that of the healthy control.[6]

Restoring optimal pulmonary function and evasion of any side effect of the used drugs are the prime objectives of the anti-asthma medication to achieve healthy active individual. Asthma severity determine, to a great extent, the type and frequency of anti-asthma drugs. Recent guidelines for management of bronchial asthma encourage the utilization of anti-inflammatory (corticosteroids and non-steroidal drugs) as well as bronchodilator inhaler for the prophylaxis of persistent asthma and management of acute attacks exacerbation.[7] A possible association was postulated between increased dental caries incidence and bronchial asthma particularly in children either directly via biological pathways or indirectly under the effect of used anti-asthma medicament, which could leave its negative effect mainly on saliva secretion and composition.[8]

Multiple factors in the bio-fluid of saliva found to play an important biological defensive mechanism against dental caries.[9] The secretory immunoglobulin A (sIgA) presents the most abundant immunoglobulin in human saliva, which imbed microbial adherence to the tooth structure, reduces bacterial aggregation, and antagonizes bacterial toxins and enzymes. Furthermore, salivary ά-amylase was also suggested to be able to

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govern the process of dental plaque formation and further microbial adhesion. Low levels of salivary ά-amylase claimed to encourage dental caries progression particularly, in susceptible children.[10] Salivary immunoglobulins and enzymes' secretion is controlled by β-adrenergic receptors where chronic stimulation, as with β-agonist antiasthmatic drugs, proposed to be associated with not only reduction but also alteration in salivary proteins' secretion.[11] Another important mechanism to guard against initiation and progression of dental caries is the preservation of relatively neutral saliva pH via different buffering systems. Alteration in the former mentioned balance, as expected to accompany the use of anti-asthma medications, would imbed one of the innate oral defences against oral and dental diseases.[12] In addition, the salivary flow not only provides washing effect that cleans oral and dental surfaces but also nourish the oral environment with variant elements necessary to create adequate protection against dental caries. Asthmatic patients frequently report decreased saliva secretions and concomitant oral complications.[13]

Scanty studies focused on the correlation between salivary characteristics of asthmatics and oral manifestations particularly in asthmatic children.[6,14] Understanding the impact of bronchial asthma on dental health would aid to provide comprehensive dental management and early interprofessional consultation. Therefore, this study was conducted to assess the dental caries experience of children suffering from bronchial asthma and the possible association between different salivary factors and the extent of dental caries in asthmatic children. The null hypotheses tested that no association could be found between changes in saliva of children suffering from bronchial asthma and increased risk of dental caries.

Materials and Methods

Study Design

A total of 120 participants aged from 4- to 12-year-old were enrolled in the present study during the period from September 2016 to January 2017. The sample consisted of 60 children (29 females and 31 males) formerly diagnosed with chronic asthma but no other systemic illness other than the asthma condition and 60 healthy children as a study control. Asthmatic children were recruited from the outpatients' clinic of Makkah Maternity and Children Hospital. Participants with persistent chronic asthma were further subdivided into mild, moderate and severe asthmatics ($n = 20$) by pediatric specialist according to severity of symptoms, acute exacerbation and frequent nocturnal symptoms.[15] The ethical approval to conduct this study was obtained from the institutional review board UQU DENT-IRB and informed consent was collected from each caregiver before including the children into the study.

Dental Examination

Through dental examination of each participant was conducted to evaluate the oral health condition while sitting on an ordinary chair using sterile disposable diagnostic tools by the same examiner. The dental caries experience was assessed according to "WHO recommendations 2013".[16] For every child, the deft/DMFT indices were calculated separately, where (d/D) carious tooth, (e/M) indicated for extraction or missing tooth due to caries and (f/F) filling due to caries in primary or permanent teeth, respectively.

Stimulated Salivary Flow Rate

Following the dental examination, stimulated saliva was collected 2 hours after breakfast from 9- to 10-AM to reduce the effect of circadian variation.[17] The children were asked to set in an upright position with the head bowed partly forward. About 1 g paraffin wax was given for each child to chew on it for 1 minute then asked to frequently deposit the collected saliva into graduated plastic container. After 5 minutes, the volume of the collected saliva was measured and divided by time to estimate the salivary flow rate per individual (mL/minute).

Saliva pH Measurement

The saliva samples were immediately analyzed following their collection to evaluate the corresponding pH using digital salivary pH meter (Adwa instruments Kft, Szeged, Hungary). According to the manufacturer instructions, one mL of saliva was dispensed on pH-sensitive electrode and the reading left few seconds for stabilization then recorded per sample. Following each reading, gauze moistened with distilled water was used to clean the pH-electrode, which then was immersed in standard solution of pH 7 to be ready for the next reading.

Salivary IgA and α-Amylase Determination

The saliva samples were centrifuged at 3,000 rpm for 15 minutes then the saturate was stored at –70°C till analysis. The concentration of sIgA (μg/mL) was measured using DRG® ELISA kit for sIgA (DRG International Inc., USA) and the salivary ά-amylase (U/mL) was measured using DRG® ELISA kit for ά-amylase (DRG International Inc., USA) following the manufacturer's directions.

Statistical Analysis

The collected data were statistically analyzed using SPSS v.23 program to check for significance at $p \leq 0.05$. Student's *t* test was used to search significance between asthmatics and the healthy control group regarding the effect of different saliva variables. The impact of the asthma condition severity on different variables (deft/DMFT, saliva flow, saliva pH, sIgA and α-amylase mean values) was examined using one-way ANOVA test followed by multiple comparisons Tukey's *post hoc* test.

Results

The age mean and SD were 7.38 ± 2.83 and 8.38 ± 3.03 for the control and asthmatic groups, respectively ($p > 0.05$). The results of the study are presented in Tables 1 and 2. The deft mean scores of the asthmatics presented statistically significant higher mean values compared to that of the healthy controls ($p \leq 0.05$). On the other hand, the flow rate and sIgA level showed statistically significant lower mean values in contrast to the control group

Table 1: Different variables among asthmatics and control groups ($n = 60$ per group)

Variable		*Control*	*Asthmatics*
Gender	Female	27 (23%)[a]	29 (24%)[a]
	Male	33 (28%)[a]	31 (26%)[a]
Age		7.38 ± 2.83[a]	8.38 ± 3.03[a]
Deft		4.02 ± 2.49[a]	6.77 ± 1.69[b]
DMFT		1.88 ± 1.18[a]	2.34 ± 1.23[a]
Flow rate (mL/minute)		1.75 ± 0.63[a]	0.84 ± 0.20[b]
pH		6.41 ± 2.43[a]	6.03 ± 1.58[a]
sIgA (μg/mL)		83.04 ± 6.42[a]	29.42 ± 6.31[b]
ά-Amylase (U/mL)		79.59 ± 7.03[a]	80.75 ± 6.76[a]

Different lower case alphabets in superscript in the same row indicate significance

Table 2: Different variables among mild, moderate and severe asthmatics

Variable		*Mild*	*Moderate*	*Severe*
Gender	Female	12 (20%)[a]	11 (18%)[a]	6 (10%)[a]
	Male	8 (13%)[a]	9 (15%)[a]	14 (23%)[a]
Age		7.88 ± 2.21[a]	8.46 ± 1.98[a]	8.74 ± 2.09[a]
Deft		5.75 ± 1.48[a]	6.40 ± 1.67[a]	8.15 ± 0.81[a]
DMFT		2.40 ± 1.72[a]	2.10 ± 1.02[a]	2.55 ± 1.39[a]
Flow rate (mL/minute)		1.05 ± 0.09[a]	0.84 ± 0.20[b]	0.64 ± 0.20[c]
pH		6.39 ± 2.11[a]	6.18 ± 1.37[a]	5.52 ± 1.74[a]
sIgA (µg/mL)		33.13 ± 5.13[a]	31.53 ± 5.18[a]	23.61 ± 5.33[b]
ά-Amylase (U/mL)		76.65 ± 6.81 [a]	80.15 ± 8.23[a]	82.78 ± 8.69[a]

Different lower case alphabets in superscript in the same row indicate significance

($p \leq 0.05$). Severe asthmatics presented significantly the least mean value of saliva flow rate and sIgA compared to that of mild and moderate asthmatics ($p \leq 0.05$). The sIgA of asthmatic children yielded statistically significant negative correlation with deft and DMFT ($p \leq 0.05$). Both saliva pH nd salivary α-amylase values showed statistically in-significant difference between the test groups ($p > 0.05$).

Discussion

Many speculations were suggested as the possible senses behind dental caries experience in asthmatic patients; however, scanty studies focused on the associative factors in asthmatics and children in particular. The results of the present study reject the null hypothesis and disclose that certain changes in the saliva of children suffering from bronchial asthma found to be resposible for the increased risk of dental caries.

Despite different indeces developed for dental caries assessment, the WHO recognized the deft and the DMFT indeces as strong reliable and repreducable mean of dental caries detection and further comparison between groups.[18] Assessment of stimulated salivary flow rate is considered a highly reliable technique in systemic diseases and conditions expected to be associated with a degree of reduced flow or affected saliva secreation.[19] The use of pH meter as a quantitative measure of saliva buffer capacity, found to be able to reduce the inherited subjective deviation of the colourimetric systems, accordingly, considered as a valid mean in accurate determination of salivary.[20]

The results of this study revealed significant increase in dental caries experience of asthmatic children where with the increase in severity of asthma condition, a higher dental caries would be experienced by the asthmatics particularly the primary dentition without significant adverse effect as the children mature.[7] Similar findings were reported by other researchers that children with bronchial asthma found to be at higher risk for increased dental caries.[21] The results of a study by Stensson et al. also indicated that preschool children with asthma have a higher prevalence of caries than children without asthma.[23] Reddy et al. added also that with the increase in asthma severity, there is increase in dental caries affection.[24] It was also reported that asthma condition would double the risk for dental caries.[25] The increase in caries experience of asthmatics could be attributed to number of reasons. The condition itself and the anti-asthmatic medicament frequently claimed to be of prime association with elevated dental caries record.[11,22] The β2-agonists bronchodilator used to relieve asthma symptoms either in syrup or dry-powder inhaler form were highly linked to higher caries susceptability of asthmatics particularly to manage the nocturnal asthma symptoms in children.[7,24,26] Either directly through being sugar added or indirectly via the adverse effect of beta 2 agonist anti-asthmatics in reducing the salivary flow rate and composition.[27]

Multiple factors in the saliva of the asthmatics presented possible association with increased dental caries. Similar to the finding of the present study, the saliva flow rate of asthmatic children reported significant reduction. The normal average of salivary flow rate estimated to range from 1.5–1.8 mL/minute.[28] Ultered flow rate found to develop due to the oral breathing habit accompany asthmatic condition in trial to increase air ingress particularly during attacks or in case of nasal obstruction. Furthermore, this impairment of the saliva secretion rate and composition could possibly result from the down-regulation of β-receptors caused by beta 2 agonist treatment as well as the frequent use of anti-histaminic drugs.[29] The net dimish of the salivary flow of asthmatic children would prohibit the protective effect of saliva against dental caries.[30] The reduction in saliva flow would not only affect the bioavailability of calcium and phosphrous ions necessary for remineralizing affected surfaces, but also debrive the oral environment from the saliva mechanical washing effect and thrust asthmatic patient for increased fluid consumption, sugar-sweetened beverage in particular.[29,31]

In addition, the results of this study presented significant decrease in sIgA mean level of the asthmatic children that affected by asthma severity with further significant negative correlation with deft and DMFT mean score. Ultered saliva composition mainly interm of significant decrease in the sIgA mean level, observed to be acompained with subsequent affection of the immune response and increased dental caries progression.[32] The sIgA dominates immunoglobulins secreated into the saliva thus accounted for the major role of defence against bacterial adhesion and dental plaque formation. It has been suggested that the content of sIgA could be considered as genetic or environmental determinant factor predesposing to dental caries andbronchial asthma as well as posses leading function in the immune system.[6] Furthermore, other researchers reported that the use of corticosteroids as anti-asthmatic inhalers found to be able to reduce the total content of sIgA.[33,34]

Former studies postulated a possible association between salivary ά-amylase and increased dental caries acivity as a result of its ability to hydrolyze dietry starch providing more glucose within the plaque matrix in proximity to the tooth surface.[10,35] However, the present study observed insignificant difference compared to the control group. This could be attributed to the difference in

the age range of the study sample and the extent of affected flow as well as saliva composition in asthmatic children. Furthermore, multiple saliva constituents and immunologic factors could be related to oral microbs growth and multiplication where certain components as sIgA and IgG showed augmenting or antagonizing impact on α-amylase mechanism of action, thus enhances or undermind the association between salivary α-amylase and dental caries activity.[35]

Although salivary pH plays critical role in development and progression of dental caries in asthmatic children,[36] our findings couldn't reveal significant reduction in the salivary pH. This could be attributed to to the variation in the degree of patients compliance with the theraputic regimen as well as the difference in the mode of saliva samples' collection and in the present study, the procedure was not attemped following the use of the anti-asthmatic medicaments.[37]

Conclusion

It can be concluded that:

- Reduced salivary flow rate and the immunoglobulin A (sIgA) level showed strong association with increased dental caries experience in asthmatic children particularly in primary dentition.
- Severe asthma condition showed the most reduced saliva flow rate and the least sIgA level.

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