Association between Mouth Breathing and Atopic Dermatitis in Japanese Children 2–6 years Old: A Population-Based Cross-Sectional Study

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Abstract

As mouth breathing is associated with asthma and otitis media, it may be associated with other diseases. Therefore, this population-based cross-sectional study evaluated the association of mouth breathing with the prevalences of various diseases in children. Preschool children older than 2 years were included. A questionnaire was given to parents/guardians at 13 nurseries in Tokushima City. There were 468 valid responses (45.2%). We defined a subject as a mouth breather in daytime (MBD) if they had 2 or more positive items among the following 3 items: “breathes with mouth ordinarily,” “mouth is open ordinarily,” and “mouth is open when chewing.” We defined subjects as mouth breathers during sleep (MBS) if they had 2 or more positive items among the following 3 items: “snoring,” “mouth is open during sleeping,” and “mouth is dry when your child gets up.” The prevalences of MBD and MBS were 35.5% and 45.9%, respectively. There were significant associations between MBD and atopic dermatitis (odds ratio [OR]: 2.2, 95% confidence interval [CI]: 1.2–4.0), MBS and atopic dermatitis (OR: 2.4, 95% CI: 1.3–4.2), and MBS and asthma (OR: 2.2, 95% CI: 1.2–4.0). After adjusting for history of asthma and allergic rhinitis; family history of atopic dermatitis, asthma, and allergic rhinitis; and nasal congestion; both MBD (OR: 2.6, 95% CI: 1.3–5.4) and MBS (OR: 4.1, 95% CI: 1.8–9.2) were significantly associated with atopic dermatitis. In preschool children older than 2 years, both MBD and MBS may be associated with the onset or development of atopic dermatitis.
Introduction

The prevalence of mouth breathing among children remains controversial but is at most reported to be 50–56% [1–8]. Mouth breathing is defined as using the mouth alone or the mouth and nose instead of the nose alone for respiration for longer than 6 months [9]. Mouth breathing is thought to be caused by mechanical factors such as septal deviation and adenotonsillar hyperplasia, inflammatory diseases such as allergic rhinitis, congenital malformation, and behavioral mouth breathing [9, 10].

The functions of the nasal cavity are air-conditioning, olfaction, and defense [11], but mouth breathing causes environmental air to bypass these nasal functions, allowing air to directly enter the lower respiratory tract, which can cause airway hyperreactivity and chronic bronchial inflammation [12–14]. Two case-control studies showed that children suffering from asthma exhibit more mouth breathing behaviors than controls [15, 16]. Meanwhile, a cohort study revealed that the risk of otitis media with effusion is 2.4 times higher in mouth breathers than nose breathers [17].

In addition, mouth breathing might be associated with skin diseases, given its previously demonstrated relationships with periodontal disease and enlarged tonsils. Periodontal disease is associated with chronic skin diseases such as chronic urticaria [18], chronic pigmented purpura [19], and chronic nodular prurigo [20]. Mouth breathers had an increased risk of gingivitis in a case-control study [21], while patients suffering from adenotonsillar hypertrophy, which is a cause of mouth breathing, have an increased risk of periodontal disease, which improves after adenoidectomy [22]. In addition, Valera et al. reported that children aged 3–6 years with enlarged tonsils had a significantly increased risk of mouth breathing [23]. Streptococcal tonsillitis is associated with psoriasis [24], while some reports indicate tonsillectomy improves psoriasis [25, 26].

However, no population-based studies have investigated the relationship between mouth breathing and the prevalences of pediatric diseases, including atopic dermatitis, which is a highly prevalent skin disease in children [27].

Accordingly, this study investigated the relationship of mouth breathing with the prevalences of various diseases including atopic dermatitis by using a questionnaire targeting preschool children in day nurseries.

Materials and Methods

Design, setting, and participants

Aimed to have a total of 600 respondents, we targeted preschool children aged 2–6 years who attended day nurseries in Tokushima City. The questionnaire was distributed at 13 randomly selected day nurseries in Tokushima City. We distributed anonymous questionnaires to the parents or guardians from November 27 to December 16, 2013. The questionnaires were submitted through collection boxes in each day nursery.

This was a population-based cross-sectional study performed with the permission of the Ethics Committee of the Tokushima University Hospital. After obtaining written informed consent from the head of each day nursery, we distributed the questionnaires to parents/guardians attached with an explanatory leaflet specifying that their submission of the questionnaire was considered consent. Within the leaflet, we also informed the parents/guardians that some, as yet unknown, behavioral habits might contribute to the development of some diseases; however, we did not provide information regarding the specific potential associations.
Questionnaire

The questionnaire included questions on the following: age, sex, smoking habits of family members, behavioral habits, present and previous diseases, and present and previous diseases of parents. A multiple choice question was used to collect information about present diseases, including allergic rhinitis, chronic sinusitis, asthma, chronic bronchitis, pollinosis, atopic dermatitis, tonsillitis, otitis media, chronic headache, proteinuria, and hematuria. In addition to the present diseases, previous diseases included acute sinusitis, acute otitis media, chronic otitis media, pneumonia, and meningitis. As some cases of allergic rhinitis are pollinosis [28], we treated pollinosis as allergic rhinitis. Excluding mouth breathing, which is described in the next section, we collected information about the following behavioral habits: regular bedtime and rising time, sleeping hours, sleeping posture, pacifier use, and dietary habits including mastication and food and drink preferences.

Mouth breathing criteria

Although there is no widely adopted questionnaire for evaluating mouth breathing, we prepared the following 3 items for detecting mouth breathers in daytime (MBD) (Table 1):

- “breathes with mouth ordinarily,” “mouth is open ordinarily,” and “mouth is open when chewing.” These items were developed with reference to generally used methods including the Glatzel mirror, lip closure, and the water test [29]. “Breathes with mouth ordinarily” corresponds to the Glatzel mirror, which judges mouth breathing by vapor emanating from the mouth using a mirror placed below the child’s nose. “Mouth is open ordinarily” corresponds to lip closure, which is determined according to soft contact between the upper and lower lips. “Mouth is open when chewing” corresponds to the water test, in which children hold some water in their mouth while keeping their lips closed without swallowing for 3 minutes. The necessity of opening the mouth during mastication suggests the child is not in the habit of complete nose breathing. Children who met 0–1 and 2–3 of the above criteria were considered nasal breathers in daytime (NBD) and MBD, respectively.

We adopted the following 3 items to detect mouth breathers during sleep (MBS): “snoring,” “mouth is open during sleep,” and “mouth is dry when your child gets up.” Snoring is significantly associated with MBD and MBS [5, 30]. Dry mouth is caused by dry air passing through the mouth unless a loss of saliva occurs [31]. Children who met 0–1 and 2–3 criteria were considered nasal breathers during sleep (NBS) and MBS, respectively.

Table 1. Questionnaires for mouth breathing.

| Questions                     | MBD Items | Choices                        |
|-------------------------------|-----------|--------------------------------|
| Breathes with mouth ordinarily| Nose usually | Mouth usually Mouth Sometimes open Often open Nose and mouth Always open |
| Mouth is open ordinarily      | Usually closed | Sometimes open Often open Always open |
| Mouth is open when chewing    | Usually closed | Usually open Both are applicable |

| Questions                     | MBS Items | Choices                        |
|-------------------------------|-----------|--------------------------------|
| Snoring                       | Not at all Not usually | Sometimes Often |
| Mouth is open during sleep    | Not at all Not usually | Sometimes Often |
| Mouth is dry when your child gets up | Wet A little dry Very dry |

Underlined and non-underlined choices were considered positive and negative for mouth breathing, respectively. MBD: mouth breather in daytime, MBS: mouth breather during sleep.

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For each item, we defined positive or negative choices for mouth breathing before distributing the questionnaire. As shown in Table 1, the underlined and non-underlined choices were defined as positive and negative for mouth breathing, respectively. We did not indicate in the questionnaire which questions were used to analyze mouth breathing or which choices were used to determine mouth breathing.

Complete mouth breathers (CMB) were defined as children who met the criteria for both MBD and MBS, partial mouth breathers (PMB) met the criteria for either MBD or MBS, and complete nasal breathers (CNB) met the criteria for both NBD and NBS.

Because nasal congestion, which is the main symptom of rhinitis and sinusitis, is an important cause of mouth breathing, we included an item for “nasal congestion”; it was assessed as negative only if “not blocked unless cold” was selected and assessed as positive if “often blocked” or “always blocked” was selected.

Genetic factors were considered positive if the parents selected the corresponding disease from among present and/or previous diseases, because atopic dermatitis and asthma improve naturally with age and allergic rhinitis is classified as intermittent, seasonal, or persistent according to the nature of the allergen. Smoking was categorized according to whether family member(s) smoked around the children or not.

Statistical analysis

Statistical analyses were performed by using SPSS version 21 (IBM Corp, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range (IQR).

For univariate analysis, categorical variables such as habits and disease presence were analyzed by Pearson’s χ² tests or Fisher’s exact tests where appropriate. The results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). To adjust the ORs of MBD and MBS with respect to disease prevalence, the Mantel–Haenszel test was performed using variables with \( p < 0.25 \) in univariate analysis as potential confounders.

For multivariate analysis, forward stepwise multiple logistic regression was performed by using breathing pattern (i.e., MBD or MBS) as the dependent variable and categorical variables showing \( p < 0.25 \) in univariate analysis as independent variables. Bonferroni corrections for multiple comparisons were made as a post hoc analysis. The level of significance was set at \( p < 0.05 \) except in cases of multiple comparisons, in which \( p < 0.016 \) was used.

We used the phi coefficient to indicate the effect size in the Pearson’s χ² test. For statistical power, we performed post hoc power analysis using G*power (ver. 3.1.9.2, Erdfelder, Faul and Buchner, Germany) [32].

Results

We distributed questionnaires to 1036 subjects from November 27 to December 16, 2013 and collected 552 responses for a response rate of 53.3%. No reminder letters were distributed. Thirteen responses were excluded because of age: 11 were outside the target age range and 2 had no age given. A further 71 responses were excluded because of at least one unanswered question. Therefore, a total of 468 valid responses were collected for a response rate of 45.2%.

The subjects’ characteristics are shown in Table 2. Mean age was 4.5 ± 1.2 years with a median of 4.5 years (IQR: 3.4–5.5 years). The subjects were divided into 3 groups according to the main diseases reported: atopic dermatitis, asthma, and allergic rhinitis. Children with atopic dermatitis were significantly associated with a history of asthma and/or allergic rhinitis. In contrast, asthmatic children were significantly associated with a history of allergic rhinitis, atopic dermatitis, and/or pneumonia. The most afflicted children were those with allergic rhinititis,
who had a history of all documented conditions except tonsillitis. Each group had a family history of their condition, and the atopic dermatitis group was also significantly associated with a family history of allergic rhinitis.

The results show that 57.5% of the children had substantial nasal breathing difficulties, including CMB (23.9%) and PMB (33.5%). The symptoms appeared to be more frequent at night; 45.9% were MBS compared to 35.5% who were MBD (Table 3).

Atopic dermatitis was significantly associated with both MBD and MBS ($p = 0.001$ and $p = 0.002$, respectively). Asthma was significantly associated with only MBD ($p = 0.013$), while allergic rhinitis was significantly associated with both MBD and MBS ($p = 0.035$ and $p = 0.006$, respectively). Nasal congestion was significantly associated with a risk of all 3 diseases, which was considered a confounder (S1 Appendix). Also, nasal congestion, which was present with $[4/97 (4.1\%)]$ and without $[1/371 (0.3\%)]$ chronic sinusitis, was associated with chronic sinusitis (OR: 15.9, 95% CI: 1.8–144.1, $p = 0.007$, Fisher’s exact test).

According to the results of the univariate analysis, we adopted previous disease (i.e., asthma and allergic rhinitis), family history of disease (i.e., atopic dermatitis, asthma, and allergic}

### Table 2. Characteristics of total subjects and subjects by disease.

|                      | Total $n$ (%) | Atopic dermatitis $n$ (%) | Asthma $n$ (%) | Allergic rhinitis $n$ (%) |
|----------------------|--------------|--------------------------|---------------|--------------------------|
| **Age (years)**      |              |                          |               |                          |
| 2                    | 62 (13.2)    | 9 (14.5)                 | 8 (12.9)      | 5 (8.1)                  |
| 3                    | 117 (25.0)   | 13 (11.1)                | 8 (6.8)       | 12 (10.3)                |
| 4                    | 111 (23.7)   | 10 (9.0)                 | 14 (12.6)     | 14 (12.6)                |
| 5                    | 106 (22.6)   | 17 (16.0)                | 10 (9.4)      | 15 (14.2)                |
| 6                    | 72 (15.4)    | 10 (13.9)                | 6 (8.3)       | 15 (20.8)                |
| Total                | 468 (100.0)  | 59 (12.6)                | 46 (9.8)      | 61 (13.0)                |
| **Sex**              |              |                          |               |                          |
| Male                 | 253 (54.1)   | 33 (55.9)                | 28 (60.9)     | 45 (73.8)**              |
| **History**          |              |                          |               |                          |
| Atopic dermatitis    | 72 (15.4)    | -                        | 15 (32.6)**   | 23 (37.7)**              |
| Asthma               | 68 (14.5)    | 20 (33.9)**              | -             | 17 (27.9)**              |
| Allergic rhinitis    | 85 (18.2)    | 25 (42.4)**              | 15 (32.6)**   | -                        |
| Pneumonia            | 55 (11.8)    | 6 (10.2)                 | 10 (21.7)*    | 12 (19.7)*               |
| Tonsillitis          | 59 (12.6)    | 6 (10.2)                 | 5 (10.9)      | 11 (18.0)*               |
| Chronic otitis media | 36 (7.7)     | 4 (6.8)                  | 4 (8.7)       | 10 (16.4)*               |
| **Family history**   |              |                          |               |                          |
| Atopic dermatitis    | 102 (21.8)   | 36 (61.0)**              | 9 (19.6)      | 15 (24.6)                |
| Asthma               | 81 (17.3)    | 14 (23.7)*               | 21 (45.7)**   | 14 (23.0)*               |
| Allergic rhinitis    | 312 (66.7)   | 47 (79.7)*               | 33 (71.7)     | 57 (93.4)**              |
| **Smoking**          |              |                          |               |                          |
| Smokes around children | 33 (7.1)  | 4 (6.8)                  | 4 (8.7)       | 1 (1.6)*                 |
| Any smoker           | 215 (45.9)   | 24 (40.7)                | 21 (45.7)     | 26 (42.6)                |

History of atopic dermatitis, asthma, and allergic rhinitis included both present and previous disease. $P$-values were calculated using Pearson’s $\chi^2$ test.

$^5$: Fisher’s exact test.

$^a$ $p < 0.25$,

$^* p < 0.05$,

$^{**} p < 0.01$,

$^{***} p < 0.001$

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rhinitis), and nasal congestion as confounding factors for atopic dermatitis. Meanwhile, previous disease (i.e., atopic dermatitis, allergic rhinitis, and pneumonia), family history of disease (i.e., asthma), and nasal congestion were adopted as confounding factors for asthma. Because nasal congestion can induce mouth breathing and is one of the main symptoms of allergic rhinitis, we excluded allergic rhinitis from subsequent analyses. After adjusting for confounders, atopic dermatitis was significantly associated with risks of both MBD (OR: 2.6, 95% CI: 1.3–5.4, \( p = 0.010 \)) and MBS (OR: 4.1, 95% CI: 1.8–9.2, \( p = 0.001 \)), although asthma was not significantly associated with a risk of MBD (OR: 1.3, 95% CI: 0.7–2.7, \( p = 0.508 \)). Multiple logistic regression for atopic dermatitis was subsequently performed by including the categorical variables listed above. The ORs of MBD and MBS for atopic dermatitis were 2.2 (95% CI: 1.2–4.2) and 2.7 (95% CI: 1.4–5.3), respectively (Table 4); these values were lower than those for

### Table 3. Association between mouth breathing and disease prevalence.

|          | Total | Atopic dermatitis | Asthma | Allergic rhinitis |
|----------|-------|-------------------|--------|-------------------|
|          | n = 468 (% | n = 409 (%) | n = 59 (%) | OR | 95% CI | n = 422 (%) | n = 46 (%) | OR | 95% CI | n = 407 (%) | n = 61 (%) | OR | 95% CI |
| **MBD** |       |                   |        |                  |       |                   |        |                  |       |                   |        |                  |       |                   |
| Positive | 166   | 134               | 32     | 2.43             | 1.40–4.23** | 142 | 24     | 2.15             | 1.17–3.97* | 137 | 29     | 1.79             | 1.04–3.07* |
|          | (35.5) | (80.7)            | (19.3) |                  |               | (85.5) | (14.5) |                  |               | (82.5) | (17.5) |                  |           |
| Negative | 302   | 275               | 27     | 1.37             | 1.34–4.18**  | 280 | 22     | 1.20             | 0.65–2.20  | 270 | 32     |                  |           |
|          | (64.5) | (91.1)            | (8.9)  |                  |               | (92.7) | (7.3)  |                  |               | (89.4) | (10.6) |                  |           |
| **MBS** |       |                   |        |                  |       |                   |        |                  |       |                   |        |                  |       |                   |
| Positive | 215   | 177               | 38     | 2.37             | 1.34–4.18**  | 192 | 23     | 1.20             | 0.65–2.20  | 177 | 38     | 2.15             | 1.23–3.73** |
|          | (45.9) | (82.3)            | (17.7) |                  |               | (89.3) | (10.7) |                  |               | (82.3) | (17.7) |                  |           |
| Negative | 253   | 232               | 21     | 1.20             | 1.34–4.18**  | 230 | 23     | 1.20             | 0.65–2.20  | 230 | 23     |                  |           |
|          | (54.1) | (91.7)            | (8.3)  |                  |               | (90.9) | (9.1)  |                  |               | (90.9) | (9.1)  |                  |           |

\( P \)-values were calculated using Pearson’s \( \chi^2 \) test. OR: odds ratio, CI: confidence interval, MBD: mouth breather in daytime, MBS: mouth breather during sleep.

* \( p < 0.05 \),  ** \( p < 0.01 \),  *** \( p < 0.001 \).

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### Table 4. Multiple logistic regression analysis of factors associated with atopic dermatitis.

|          | MBD |          | MBS |          |
|----------|-----|----------|-----|----------|
|          | OR | 95% CI   | OR | 95% CI   |
| Mouth breathing | 2.19 | 1.15–4.15  | *  | 2.71 | 1.40–5.25  |
| History of allergic rhinitis | 4.67 | 2.31–9.43  | *** | 4.69 | 2.32–9.49  |
| History of asthma | 4.71 | 2.23–9.98  | *** | 5.15 | 2.42–10.99 |
| Parental history of atopic dermatitis | 12.51 | 6.24–25.05 | *** | 13.56 | 6.69–27.47 |

Breathing pattern (i.e., MBD or MBS) was the dependent variable, and the following variables showing \( p < 0.25 \) in the univariate analysis were included as independent variables: previous disease (i.e., asthma and allergic rhinitis), parental disease history (i.e., atopic dermatitis, asthma, and allergic rhinitis), and nasal congestion (\( n = 468 \)). MBD: mouth breather in daytime, MBS: mouth breather during sleep, OR: odds ratio, 95% CI: 95% confidence interval.

* \( p < 0.05 \),  ** \( p < 0.01 \),  *** \( p < 0.001 \).

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family history of atopic dermatitis and history of asthma and allergic rhinitis. Nasal congestion and parental history of asthma and allergic rhinitis were not significant risk factors.

The effect sizes of MBD and MBS for atopic dermatitis were 0.149 and 0.141, respectively, and 0.897 and 0.862, respectively, represented the statistical power in the post hoc analysis, indicating sufficient power.

Atopic dermatitis was present in 7.0% of children with CNB (n = 199), 12.7% of children with PMB (n = 157), and 22.3% of children with CMB (n = 112) (p < 0.001). The prevalence of atopic dermatitis in CMBs was higher than that in PMBs (p = 0.038), but the difference was not significant after Bonferroni correction.

Discussion

The results of the present study indicate mouth breathing is significantly associated with atopic dermatitis and asthma. In particular, atopic dermatitis was significantly associated with both MBD and MBS after adjusting for confounding factors. Moreover, the prevalences of these diseases showed an increasing trend with an increasing extent of mouth breathing. To our knowledge, this is the first study to evaluate the impact of breathing patterns on the prevalence of atopic dermatitis. Although two studies report that mouth-breathing children with positive skin-prick test results have higher prevalences of asthma and sleep apnea than those with negative results [9, 33], they did not compare mouth breathers with nasal breathers.

No previous study has analyzed the prevalence of mouth breathing among Japanese children. In the present study, the prevalences of MBD and MBS were 35.5% and 45.9%, respectively; however, these results were based on a questionnaire that has not been assessed for validity. The studies from other countries report a wide range of the prevalence of mouth breathing, 4–56% [1–8]. Brazil has the highest prevalence, which exceeds 50% based on clinical assessment [1–3]. On the other hand, the lowest prevalence is in India, at 4–7% based on clinical assessment [6–8]. The prevalences of mouth breathing in England and New Zealand are 23% and 19%, respectively [4, 5]. However, direct comparison among studies is difficult owing to varying criteria. Standardized criteria for mouth breathing using clinical assessment and questionnaires are required to more precisely investigate differences in mouth breathing prevalence.

Atopic dermatitis is a chronic skin disorder characterized by pruritus and inflammation that mostly develops during childhood and is strongly associated with the allergic history of patients and relatives [34]. Filaggrin, which is encoded by the FLG gene, is a crucial protein for skin barrier function [35, 36]. Two meta-analyses show that children with an abnormal FLG gene are 3.12–4.78 times more likely to have atopic dermatitis than normal subjects [37, 38]. On the other hand, the prevalences of chronic pediatric diseases, including atopic dermatitis as well as asthma and allergic rhinitis, vary greatly worldwide [27]. The prevalences of these diseases have increased in the late 20th century [39–41], although this trend has not held true in the last 10 years [39, 42]. These findings suggest that, in addition to genetic factors, environmental factors play important roles in these diseases.

This was a population-based cross-sectional study; therefore, causal relationships cannot be determined. However, if mouth breathing is shown to contribute to atopic dermatitis in future cohort studies, guidance to avoid mouth breathing should be provided to children and parents/guardians to prevent atopic dermatitis. Furthermore, otolaryngologist help should be considered, as necessary, if children find it difficult to quit mouth breathing.

It is possible that periodontal disease and/or tonsillitis might mediate the mechanism underlying any association between mouth breathing, as an environmental factor, and atopic dermatitis [18–26]. Satoh et al. suggested that immune reactions mediated by bacterial–immune
complexes, superantigens, or toll-like receptors might induce skin diseases [20]. However, the present questionnaire did not collect periodontal information. Furthermore, although the present results showed no significant relationship between history of tonsillitis and the prevalence of atopic dermatitis, inquiring about the number of repeated tonsillitis episodes might have revealed an association. On the other hand, it is possible that children could have mild nasal congestion unnoticed by their guardians. Thus, case–control studies with otolaryngological diagnostic tests are required to confirm the relationship between mouth breathing and atopic dermatitis. Furthermore, sleep disturbance due to the intense pruritus of atopic dermatitis [43] can cause daytime sleepiness [44], which might in turn cause behavioral mouth breathing.

According to the Japanese Ministry of Health, Labour, and Welfare, the prevalences of atopic dermatitis in 3- and 6–7-year-old children are 13.2% and 11.8%, respectively [45]. Meanwhile, the prevalence of asthma in a study of 34,699 children aged 4–5 years at randomly selected nurseries in Japan was 11.2%, and the lifetime prevalences of atopic dermatitis, asthma, and allergic rhinitis were 16.0%, 16.1%, and 17.6%, respectively [46]. In the present study, the prevalences of atopic dermatitis, asthma, and allergic rhinitis were 12.6%, 9.8%, and 13.0%, respectively; the lifetime prevalences were 15.4%, 14.5%, and 18.2%, respectively. Thus, the present results are similar to those of previous studies, suggesting the subject group is representative of Japanese children aged 2–6 years.

In this study, 45.9% of children had family members who smoked. This is similar to the prevalence of smokers among Japanese men and women 20–40 years old: 40% and 12%, respectively [47]. However, having a family member who smoked was not associated with disease prevalence. Possible reasons for this are the low rate of smokers who smoke around their children (7.1%) and parents who stop smoking when their child develops a disease.

There are some limitations in this study, as already mentioned. First, the diagnoses of atopic dermatitis and mouth breathing were dependent on the questionnaire results. Because we created the questions and criteria for mouth breathing, the lack of experimental data and questionnaire validity limits the strength of our findings. Second, the valid response rate was comparatively low at 45.2%. Third, as this was a cross-sectional study, causal relationships cannot be determined. Although we cannot exclude facial injuries affecting nasal breathing, such cases would be rare and are unlikely to affect the results. The effects of common cold and flu appear quite small, because we inquired about the normal state of the children in the questionnaire. Finally, regarding genetic factors, only the parents’ information was collected and not that of sibling or grandparents. Therefore, genetic factors may have been underestimated.

**Conclusion**
Mouth breathing is significantly associated with atopic dermatitis in Japanese preschool children aged 2–6 years. Additional case–control and cohort studies are required to confirm this relationship. Furthermore, studies targeting school children and adults would also help clarify this association.

**Supporting Information**
S1 Appendix. Association between mouth breathing and disease prevalence (full data).

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Author Contributions

Conceived and designed the experiments: HY KT. Performed the experiments: HY ST YN SK RT SY NS MK. Analyzed the data: HY SK RT SY NS MK KT AT. Contributed reagents/materials/analysis tools: KT. Wrote the paper: HY TS KT.

References

1. Abreu RR, Rocha RL, Lamounier JA, Guerra AF. Prevalence of mouth breathing among children. J Pediatr (Rio J) 2008; 84: 467–470. doi:10.2223/JPED.1806 PMID: 18830512

2. De Menezes VA, Leal RB, Pessoa RS, Pontes RM. Prevalence and factors related to mouth breathing in school children at the Santo Amaro project-Recife, 2005. Braz J Otorhinolaryngol 2006; 72: 394–399. PMID: 17119778

3. Felcar JM, Bueno IR, Massan AC, Torezan RP, Cardoso JR. Prevalence of mouth breathing in children from an elementary school. Cien Saude Colet 2010; 15: 437–444. doi:10.1590/S1413-81232010000200020 PMID: 2291186

4. Bonuck KA, Chervin RD, Cole TJ, Emond A, Henderson J, Xu L, et al. Prevalence and persistence of sleep disordered breathing symptoms in young children: a 6-year population-based cohort study. Sleep 2011; 34: 875–884. doi: 10.5665/SLEEP.1118 PMID: 21731137

5. Gill AI, Schauhency E, Galland BC. Prevalence and factors associated with snoring in 3-year olds: early links with behavioral adjustment. Sleep Med 2012; 13: 1191–1197. doi:10.1016/j.sleep.2012.05.007 PMID: 22951186

6. Garde JB, Suryavanshi RK, Jawale BA, Deshmukh V, Dadhe DP, Suryavanshi MK. An epidemiological study to know the prevalence of deleterious oral habits among 6 to 12 year old children. J Int Oral Health 2014; 6: 39–43. PMID:24653601

7. Shetty SR, Munshi AK. Oral habits in children—a prevalence study. J Indian Soc Pedod Prev Dent 1998; 16: 61–66. PMID: 11813757

8. Kharbanda OP, Sidhu SS, Sundaram K, Shukla DK. Oral habits in school going children of Delhi: a prevalence study. J Indian Soc Pedod Prev Dent 2003; 21: 120–124. PMID: 14703220

9. Barros JR, Becker HM, Pinto JA. Evaluation of atopy among mouth-breathing pediatric patients referred for treatment to a tertiary care center. J Pediatr (Rio J) 2006; 82: 458–464. PMID: 17171205

10. Trabalon M, Schaal B. It takes a mouth to eat and a nose to breathe: abnormal oral respiration affects neonates’ oral competence and systemic adaptation. Int J Pediatr 2012; 207605. Epub 2012 Jul 3. doi: 10.1155/2012/207605 PMID: 22811731

11. Elad D, Wolf M, Keck T. Air-conditioning in the human nasal cavity. Respir Physiol Neurobiol 2008; 163: 121–127. doi: 10.1016/j.resp.2008.05.002 PMID: 18568505

12. Griffin MP, McFadden ER Jr, Ingram RH Jr. Airway cooling in asthmatic and nonasthmatic subjects during nasal and oral breathing. J Allergy Clin Immunol 1982; 69: 354–359. PMID: 7069070

13. Chen WY, Chai H. Airway cooling and nocturnal asthma. Chest 1982; 81: 675–680. PMID: 7075300

14. Sue-Chu M. Winter sports athletes: long-term effects of cold air exposure. Br J Sports Med 2012; 46: 397–401. doi: 10.1136/bjsports-2011-090822 PMID: 22267570

15. Steinsväg SK, Skadberg B, Bredesen K. Nasal symptoms and signs in children suffering from asthma. Int J Pediatr Otorhinolaryngol 2007; 71: 615–621. PMID: 17275928

16. Stensson M, Wendt LK, Koch G, Oldaeus G, Birkhed D. Oral health in preschool children with asthma. Int J Paediatr Dent 2008; 18: 243–250. doi: 10.1111/j.1365-263X.2008.00921.x PMID: 18489575

17. van Bon MJ, Zielhuis GA, Rach GH, van den Broek P. Otitis media with effusion and habitual mouth breathing in Dutch preschool children. Int J Pediatr Otorhinolaryngol 1989; 17: 119–125. PMID: 2759777

18. Sonoda T, Anan T, Ono K, Yanagisawa S. Chronic urticaria associated with dental infection. Br J Dermatol 2001; 145: 516–518. PMID: 11531855

19. Satoh T, Yokozeki H, Nishioka K. Chronic pigmented purpura associated with odontogenic infection. J Am Acad Dermatol 2002; 46: 942–944. PMID: 12063498

20. Satoh T, Takayama K, Sawada Y, Yokozeki H, Nishioka K. Chronic nodular prurigo associated with nummular eczema: possible involvement of odontogenic infection. Acta Derm Venereol 2003; 283: 376–377.

21. Wagaiyu EG, Ashley FP. Mouthbreathing, lip seal and upper lip coverage and their relationship with gingival inflammation in 11–14 year-old schoolchildren. J Clin Periodontol 1991; 18: 698–702. PMID: 1820769
22. Demir UL, Celinkaya B, Karaca S, Sigirli D. The impacts of adenotonsillar hypertrophy on periodontal health in children: a prospective controlled pilot study. Am J Otolaryngol 2013; 34: 501–504. doi: 10.1016/j.amjoto.2013.04.013 PMID: 23726657

23. Valera FC, Travitzki LV, Mattar SE, Matsumoto MA, Elias AM, Anselmo-Lima WT. Muscular, functional and orthodontic changes in preschool children with enlarged adenoids and tonsils. Int J Pediatr Otorhinolaryngol 2003; 67: 761–770. PMID: 12791452

24. Gudjonsson JE, Thorarinsson AM, Sigurgeirsson B, Valdimarsson H. Streptococcal throat infections and exacerbation of chronic plaque psoriasis: a prospective study. Br J Dermatol 2003; 149: 530–534. PMID: 14510985

25. Sigurdardottir SL, Thorleifsdottir RH, Valdimarsson H, Johnston A. The role of the palatine tonsils in the pathogenesis and treatment of psoriasis. Br J Dermatol 2013; 168: 237–242. doi: 10.1111/j.1365-2133.2012.12115.x PMID: 22901242

26. Thorleifsdottir RH, Sigurdardottir SL, Sigurgeirsson B, Olafsson JH, Sigurdsdottir MI, Petersen H, et al. Improvement of psoriasis after tonsillectomy is associated with a decrease in the frequency of circulating T cells that recognize streptococcal determinants and homologous skin determinants. J Immunol 2012; 188: 5160–5165. doi: 10.4049/jimmunol.1102834 PMID: 22374436

27. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. Lancet 1998; 351: 1225–1232.

28. Yamada T, Saito H, Fujieda S. Present state of Japanese cedar pollinosis: The national affliction. J Allergy Clin Immunol 2014; 133: 632–639. doi: 10.1016/j.jaci.2013.11.002 PMID: 24361081

29. Limeira AB, Aguiar CM, de Lima Bezerra NS, Câmara AC. Association between breastfeeding and the development of breathing patterns in children. Eur J Pediatr 2013; 172: 519–524. doi: 10.1007/s00431-012-1919-x PMID: 23274436

30. Sogut A, Yilmaz O, Dinc G, Yuksel H. Prevalence of habitual snoring and symptoms of sleep-disordered breathing in adolescents. Int J Pediatr Otorhinolaryngol 2009; 73: 1769–1773. doi: 10.1016/j.ijporl.2009.09.026 PMID: 19846222

31. Verma M, Seto-Poon M, Wheatley JR, Amis TC, Kirkness JP. Influence of breathing route on upper airway lining liquid surface tension in humans. J Physiol 2006; 574: 859–866. PMID: 16690717

32. Faul F, Erdfelder E, Lang AG, Bunchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav. Res. Methods 2007; 39: 175–91. PMID: 17695343

33. Costa EC Jr., Sabino HA, Miura CS, de Azevedo CB, de Menezes UP, Valera FC, et al. Atopy and adenotonsillar hypertrophy in mouth breathers from a reference center. Braz J Otorhinolaryngol 2013; 79: 663–667. doi: 10.5935/1808-8694.20130123 PMID: 24474475

34. Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol 2014; 70: 338–351. doi: 10.1016/j.jaad.2013.10.010 PMID: 24290431

35. Irvine AD, McLean WH, Leung DY. Filaggrin mutations associated with skin and allergic diseases. N Engl J Med 2011; 365: 1315–1327. doi: 10.1056/NEJMra1101104 PMID: 21991953

36. McAleer MA, Irvine AD. The multifunctional role of filaggrin in allergic skin disease. J Allergy Clin Immunol 2013; 131: 280–291. doi: 10.1016/j.jaci.2012.12.668 PMID: 23374260

37. van den Oord RA, Sheikh A. Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis. BMJ 2009; 339: b2433. doi: 10.1136/bmj.b2433 PMID: 19589816

38. Rodríguez E, Baurecht H, Herberich E, Wagenpfeil S, Brown SJ, Cordell HJ, et al. Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disease. J Allergy Clin Immunol 2009; 123: 1361–70.e7. doi: 10.1016/j.jaci.2009.03.036 PMID: 19501237

39. Yura A, Kouda K, Iki M, Shimizu T. Trends of allergic symptoms in school children: large-scale long-term consecutive cross-sectional studies in Osaka Prefecture, Japan. Pediatr Allergy Immunol 2011; 22: 631–637. doi: 10.1111/j.1399-3038.2011.01159.x PMID: 21466587

40. Eichenfield LF, Hanifin JM, Beck LA, Lemanske RF Jr., Sampson HA, Weiss ST, et al. Atopic dermatitis and asthma: parallels in the evolution of treatment. Pediatrics 2003; 111: 608–616. PMID: 12612244

41. Hansen TE, Evjenh B, Holt J. Increasing prevalence of asthma, allergic rhinoconjunctivitis and eczema among schoolchildren: three surveys during the period 1985–2008. Acta Paediatr 2013; 102: 47–52. doi: 10.1111/apa.12030 PMID: 22994385

42. Pearce N, Alt-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2007; 62: 758–766. PMID: 17504817
43. Chamlin SL, Mattson CL, Frieden IJ, Williams ML, Mancini AJ, Cella D, et al. The price of pruritus: sleep disturbance and cosleeping in atopic dermatitis. Arch Pediatr Adolesc Med 2005; 159: 745–750. PMID: 16061782

44. Camfferman D, Kennedy JD, Gold M, Martin AJ, Lushington K. Eczema and sleep and its relationship to daytime functioning in children. Sleep Med Rev 2010; 14(6): 359–369. doi:10.1016/j.smrv.2010.01.004 PMID: 20392655

45. Takeuchi S, Esaki H, Furue M. Epidemiology of atopic dermatitis in Japan. J Dermatol 2014; 41: 200–204. doi:10.1111/1346-8138.12331 PMID: 24628069

46. Okabe Y, Adachi Y, Itazawa T, Yoshida K, Ohya Y, Odajima H, et al. Association between obesity and asthma in Japanese preschool children. Pediatr Allergy Immunol 2012; 23: 550–555. doi:10.1111/j.1399-3038.2011.01261.x PMID: 22360643

47. Japan Health Promotion and Fitness Foundation. Adult smoking rate—national health and nutrition examination survey (Ministry of Health, Labour and Welfare). 2012. Available: http://www.health-net.or.jp/tobacco/product/pd100000.html. Accessed 23 October 2014