# Prevalence and Severity of Asthma, Rhinitis and Eczema in Pre-School Children in the United Arab Emirates

By Mohammed Shamssain<sup>\*</sup>, Anisa Alhamadi<sup>±</sup>, Siba Nezar Al Afandi<sup>‡</sup>, Tasneem Naeem Awadallah<sup>‡</sup> & Shatha Naeem Awadallah<sup>§</sup>

Very few studies have been carried out on asthma and allergies in pre-schoolchildren. This is the first study of pre-school children with asthma and allergies in the United Arab Emirates. We studied 4,000 pre-schoolchildren from the United Arab Emirates: Dubai, Sharjah, Abu Dhabi, and Al-Ain. The ages of the study group were between 1-5 years, and were 2,000 boys and 2,000 girls; they were randomly selected from kindergartens and nurseries. We used the standardised International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. The mean (SD) age, height, weight and BMI were 3.3 (1.4) years, 92.0 (1.3) cm, 17.3 (5.2) kg, and 23.4 (9.3). The prevalence rates of "wheeze ever", "current wheeze", "speech limitation", "asthma", "dry night cough", and "exercise-induced asthma" were 40.4%, 43.8%, 37.6%, 26.5%, 36.1, and 37.6%, respectively. Boys had a significantly higher prevalence of wheeze ever and current wheeze than girls. Girls had a significantly higher prevalence of speech limitation than boys. The prevalence rates of "rhinitis ever", "current rhinitis", "itchy watery eyes" and "hay fever" were 42%, 40.5%, 39.1% and 46.9%, respectively. Boys had significantly higher prevalence rates of "rhinitis ever", "current rhinitis", and "itchy watery eyes" than girls. The prevalence rates of "rash ever", "current rash" and "eczema ever" were 38.9%, 33.7% and 58.0%, respectively. Boys had significantly higher prevalence rates of rash ever, current rash, and eczema ever than girls. Children who were exposed to parental smoking have significantly higher prevalence rates of asthma, wheezing, and cough than those whom were not exposed. Children who breastfed more than 10 months had a significantly lower prevalence rates of "wheeze ever", "current wheeze", "speech limitation", and "asthma", than those whom breastfed less than 10 months. The prevalence rates of asthma, rhinitis and eczema were very high. Breastfeeding was found to be protective for asthma. The study can be used as a baseline intervention project to reduce incidents of asthma and allergies in these children and to establish atopic march in order to implement strategies to improve the respiratory health and allergies in these children.

**Keywords:** asthma, wheeze, night cough, rhinitis, eczema, pre-school children, paediatric asthma

#### Introduction

The prevalence of asthma and other allergic diseases (e.g., rhinitis and eczema) has increased over the last twenty years worldwide (Barreto et al. 2006, Forno et al. 2015, Weinmayr et al. 2008, Nutten 2015). Atopy is an important risk factor for asthma, rhinitis, and eczema, related to the allergic component of these diseases

<sup>\*</sup>Researcher, Faculty of Medical Sciences, University of Newcastle upon Tyne, United Kingdom.

<sup>&</sup>lt;sup>±</sup>Clinical Pharmacist, Ministry of Health and Prevention, United Arab Emirates.

<sup>&</sup>lt;sup>+</sup>Clinical Pharmacist, Universal Hospital, Abu Dhabi, United Arab Emirates.

<sup>&</sup>lt;sup>‡</sup>Clinical Pharmacist, Nova Medical Centre, Al-Ain, United Arab Emirates.

<sup>§</sup>Clinical Pharmacist, Nova Medical Centre, Al-Ain, United Arab Emirates.

(Cohen et al. 2003, Mallol et al. 2013, Aït Khaled et al. 2009). The International Study of Asthma and Allergies in Childhood (ISAAC) documented high prevalence rates of allergic diseases and atopy in some countries like Europe, Australia, New Zealand, Brazil, Paraguay, Uruguay, Ecuador, and Peru (Forno et al. 2015, Weinmayr et al. 2008, Beasley 1998, Rosser et al. 2014). Allergic diseases are considered to arise through complex interactions between genetic susceptibility and environmental exposures (Strina et al. 2014), so that temporal trends in prevalence are most likely to be explained by changes in environmental exposure, lifestyle, and living conditions (Barreto et al. 2006).

In developed countries, over one-quarter of the population is affected by allergic diseases which are considered one of the most common problems seen by primary care physicians and pediatricians. Morbidity and school absenteeism correlates with the raised prevalence of asthma, allergic rhinitis, and atopic dermatitis in children. In children and adults, asthma is considered as one of the most widespread chronic diseases. Over the last three decades, the prevalence of asthma has grown in developed and developing countries (Al Ghobain et al. 2012).

The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire for children, and the European Community Respiratory Heath Survey (ECRHS) for adults, are standardized research instruments that add better insight into the worldwide prevalence of asthma and other allergic diseases (Asher et al. 1995, Asher et al. 2006, Al Ghobain et al. 2012).

The prevalence of asthma was decreased in children who grew up in rural settings because of the presence of endotoxin (Bateman et al. 2008). In developed countries, asthma is considered the most common respiratory disease affecting children, with 10-30% of all school age children diagnosed. Lau et al. (2002), Stewart et al. (2001), and Weiland et al. (1999) found that a maternal history of asthma is known to induce a great risk for childhood asthma, and result from environmental factors like the utero-immunologic environment which can confer additional susceptibility.

The ISAAC study indicated that there are differences in the prevalence and incidences of asthma, allergic rhino-conjunctivitis and eczema which can be considered as a result of environmental factors including economic development (Weiland et al. 2004), dietary factors (Von Mutius et al. 2000), climate (Burr et al. 2003), infections (Cauwenberge 2003), and pollens (Sibbald 1993). Godfrey (1996) showed that the U.K had the 5th highest incidence of asthma (30-35%) compared to Russia, China and Greece where they had the lowest incidence of asthma (2-5%).

Allergic Rhinitis (AR) is an autoimmune disease that presents clinically with rhinorrhea, nasal obstruction, nasal itching, and sneezing which are reversible, spontaneously or with treatment. AR in children is clinically explained as a symptomatic disorder of the nose induced by an IgE-mediated inflammation after allergen exposure of the membranes lining the nose. The subdivision of rhinitis disease includes "intermittent" and "persistent". Regarding the severity of allergic rhinitis, it has been classified into three types based on the duration and the effect of allergic rhinitis on daily activities (mild, moderate and severe) (Ciprandi et al. 1996).

AR is considered a global health problem and it is one of the most common diseases worldwide, affecting 10 to 25% of the population. Many patients do not recognize rhinitis as a disease and therefore do not consult a physician; therefore, the figures probably underestimate the prevalence of the disease (Gregory et al. 1999).

Over the last decades, an increasing prevalence of AR has been recognized (Simons 1996). According to Gregory et al. (1999), AR is one of the top ten reasons for visiting primary care clinics. AR significantly impacts the social life of patients, affects school performance (Malone et al. 1997), as well as work productivity (Renzoni et al. 1999). The cost of rhinitis is substantial (Krol and Krafchik 2006). A large variation in the prevalence of asthma and rhinitis symptoms in children throughout the world has been demonstrated by the ISAAC. In the 6- to 7-year-old age group, the prevalence of rhinitis with itchy-watery eyes "rhino-conjunctivitis" varied from 0.8% to 14.9% and in the age group of 13- to 14-year-olds, it varied from 1.4% to 39.7% (Teng et al. 2006). In school children, the overall correlation between the prevalence of asthma and rhinitis was significant.

Bosnic-Anticevich et al. (2020) have concluded that the parent-perceived burden of AR in Australian children is high and it impacts many areas of day-to-day living. Inadequate symptom control is a key driver of the extent of this impact. Opportunities to optimise the management of AR in children include the adoption of self-assessment tools to gauge and monitor the adequacy of symptom control.

Bousquet et al. (2020) have recently indicated the following facts about AR: AR is caused by immunoglobulin E (IgE)-mediated reactions to inhaled allergens and is one of the most common chronic conditions globally. AR often co-occurs with asthma and conjunctivitis, and is a global health problem causing major burdens and disability worldwide. Risk factors include inhalant and occupational allergens, as well as genetic factors. AR impairs quality of life, affects social life, school and work, and is associated with substantial economic costs. The AR and its Impact on Asthma (ARIA) initiative classified AR into intermittent or persistent and mild or moderate/severe.

Wheeze is an adventitious, high-pitched whistling sound made while breathing and is associated with difficulty breathing. Recurrent wheezing is common in young infants and toddlers, with 27% of all children having at least one wheezing episode by the age of 9 years. The initial wheezing episodes in young children are often linked to respiratory infections due to viral pathogens such as respiratory syncytial virus, rhinovirus, human metapneumovirus, and influenza virus. Bacterial colonization of the neonatal airway also may be significant in the late development of recurrent wheeze and asthma. Some 60% of children who wheeze in the first 3 years of life will have resolution of wheezing by age 6 years ("transient early wheezers") (Robinson and Singh 2012).

The characteristic of atopic dermititis (AD), a pruritic dermatitis which is localized in different areas, depends on the age of the child. The face and lower leg extensors are affected in infancy, whereas the flexural areas are commonly involved in childhood. In adulthood, however, the eruption has a more diffused distribution. Xerosis of the skin, early age of onset, and a chronic, relapsing course

are important clues to the diagnoses of eczema (Tootoonchi 2004). Exposures to oxidant air pollutants (O3 and NO2), but not PM2.5, were associated with an increased risk of incident asthma and eczema in children. This suggests that improving air quality may contribute to the prevention of asthma and other allergic diseases in childhood and adolescence.

In early life, wheeze may be attributed to a variety of causes such as respiratory infections, but data on asthma in younger pre-school children remains inadequate. However there are a few studies on the epidemiology of asthma and related symptoms in pre-school children.

Von Kobyletzki et al. (2012), conducted a cross sectional prevalence study of wheeze, rhinitis and eczema in 7,549 randomly selected Singaporean pre-school children between the ages of 4 to 6. Cumulative and past 12 months (current) prevalence of wheeze was 27.5% and 16.0%, respectively. Asthma was reported by 11.7% of the group. Current rhinitis prevalence was 25.3% and rhinoconjunctivitis was 7.6%, current chronic rash affected 13.5% of subjects, while 9.9% reported chronic rash with flexural distribution. After multivariate analysis, the main risk factor for "current wheeze" and self-reported asthma was a family history of allergy. The study showed that a considerable portion of pre-school children were affected by these allergy-associated symptoms, which supports the need for allergy education and intervention programs in this age group towards avoiding certain triggers of asthma, etc.

A study was performed by Grize et al. (2006) to analyze the prevalence of asthma and related symptoms in children younger than 5 years. A survey was conducted by interviewing the mothers of 617 children using the ISAAC questionnaire. The overall cumulative and 12 month prevalence of wheezing were 21.9% and 19.4%, respectively. The prevalence of exercise-induced wheezing, dry cough without respiratory infections or physician-diagnosed asthma were 18.9%, 11.8% and 3.9%, respectively. There was a high prevalence of history of wheezing or exercise-induced wheezing in the male sex, and in children with positive history of atopy, constant cough unrelated to respiratory infections was strongly associated. Moreover, a physician-diagnosed asthma was strongly associated with a positive history of atopy in children.

Another study was performed by Barnes, Godfrey and Martin (1998) to assess the association between eczema in early childhood, and the onset of asthma and rhinitis later in life in children. Of 3,124 children aged 1-2 years, the prevalence of eczema was 17.6% at baseline. Children with eczema had a 3-4 fold risk of developing asthma, and nearly 3-fold risk of developing rhinitis at follow-up, compared with children without eczema. Further independent risk factors increasing the odds of developing asthma were a parental history of allergic disease and a period of breast feeding shorter than 6 months. The incidence of rhinitis was increased in parental history of allergic disease. Thus, during the following 5 year period in infancy, eczema was associated with the development of asthma and rhinitis.

A cross-sectional study was carried out by Myers (2012) to evaluate the prevalence of current wheezing in pre-school children, and to examine the association between current wheezing and current rhinitis, considering its severity

and persistency. The sample was represented by 5,003 Portuguese children aged 3-5 years. Current wheezing prevalence was 24.5%, and in the previous year, 9.4% of the participants had  $\geq$  4 wheezing episodes. It was found that almost 25% of pre-school children had current wheezing which was strongly associated with rhinitis.

Gaga et al. (2007) studied the prevalence of atopic dermatitis in a sample of pre-school children aged 3-5 years. Children with atopic dermatitis presented with 32.2% affected by rhinitis and 24.2% affected by wheezing; a high prevalence of atopic dermatitis and a close relationship with rhinitis symptoms.

Another study conducted by Moss (1989) investigates whether the infants with atopic eczema were at greater risk of developing asthma and allergic rhinitis than those with non-atopic eczema. The presence of eczema was documented in children up to 2 years of age in a birth cohort study of 620 infants with a family history of atopic disease. Skin prick tests (SPTs) at 6, 12, and 24 months using six common allergens, were used to determine the sensitization status. So, in order to determine the presence of asthma and allergic rhinitis, interviews were conducted at 6 and 7 years. The study showed that within the first 2 years of life for children with eczema, SPT can provide a very important data on the risk of childhood asthma and allergic rhinitis.

Four cross-sectional surveys in 5- to 7-year-old children were conducted in seven different communities in Switzerland between 1992 and 2001 by Barnes (2012). The results showed that the increase in prevalence of asthma and hay fever in 5- to 7-year-old children living in Switzerland may have ceased, but atopic dermatitis symptoms may still have increased, especially among girls.

More and more, new-fashioned personal products, household appliances, building materials and furnishing materials have been used in residences (Al Ghobain et al. 2012, Bateman et al. 2008, Moss 1989, Gwaltney 1996), changing indoor environmental exposures in residences over the past 20 years (Bateman et al. 2008, Lau et al. 2002, Gwaltney 1996, Gwaltney et al. 1992). During the same time period in developed countries: Germany (Schiffman 1992), Italy (Girgis et al. 2007), Australia (Bateman et al. 2008, Weiland et al. 2004), and Switzerland (Bauer et al. 1973), similar exposures to modern chemicals began many years ago and have plateaued. In developing countries where home environments have recently and rapidly changed, prevalence rates of these diseases and symptoms among children appear to have been increasing (Lau et al. 2002, Stewart et al. 2001, Weiland et al. 1999, Weiland et al. 2004, Von Mutius et al. 2000).

Since 1990, several studies have been conducted on childhood asthma and related diseases or symptoms (Cauwenberge 2003, Sibbald 1993, Ciprandi et al. 1996, Proud et al. 1990, Kaufman 1986, Graf 1997, Ellegard and Karlsson 1994), and their associations with ambient environmental exposure (Ellegard and Karlsson 1999, Mallol et al. 2013, Zollner et al. 2005, Duggan et al. 2012, Poulos et al. 2005), but between 2000 and 2010, there has not been a large-scale study simultaneously conducted in urban and suburban districts. Thus, it is of interest to investigate to what extent childhood asthma prevalence has increased.

Attendance at daycare facilities is associated with a greater contact among young children, and much greater exposure to infections during childhood, in

comparison with children who stay at home (Barreto et al. 2010, Okomoto et al. 2004, Wahn and Von Mutius 2001, Swartz et al. 2019).

Few published studies have explored risk factors and prevalence of asthma and allergic diseases in pre-school children, and none has been done in the UAE. The aim of the present study was to describe the prevalence of asthma, rhinitis, and eczema among a representative sample of pre-school children living in this expanding country and identify associated risk factors, and to what extent pre-school childhood asthma and allergy has increased. It aims to report the current prevalence and severity of childhood asthma, allergies and other respiratory symptoms in pre-school children which can be used in asthma prevention programmes.

#### **Materials and Methods**

We used a validated Arabic and English version of the ISAAC questionnaire which has been used in related published papers. We added relevant questions on breastfeeding. All participants' parents verbally consented for themselves and for the pre-school children for whom they responded to questionnaires. Parents of all participants voluntarily responded to the survey. Kindergartens and nurseries have approved this procedure for obtaining consent.

We preliminarily contacted the administrations of the kindergartens/nurseries in the Emirates of Dubai, Sharjah, Abu Dhabi and Al-Ain to include all pre-school children. We visited and recommended that the child's parent fill out the questionnaire.

#### Study Design

The study involved a cluster random sample of pre-school children aged 1-5 years of age to study the prevalence and severity of asthma, rhinitis, and eczema, with a response rate of 95%.

Inclusion and Exclusion Criteria

#### <u>Inclusion Criteria</u>

- 1. Participants were enrolled pre-school children in Dubai, Sharjah, Abu Dhabi and Al Ain, UAE (nurseries and kindergartens).
- 2. Target age group was under 6 years old
- 3. Willing to participate in the study

# **Exclusion Criteria:**

- 1. Children over 6 years
- 2. Not willing to participate in the study

# Study Participants

We studied 4,000 children from nurseries and kindergartens from both genders (2,000 males and 2,000 females) from different nationalities.

# Sampling Method

We studied all children from each kindergarten/nursery in order to complete the required sample size.

An ISAAC questionnaire (Arabic and English versions) was used. After the questionnaires were collected, they were carefully checked and coded. Pearson's chi-squared ( $\chi$ 2) test was used to test for significance of difference in prevalence between different groups of children. A p-value <0.05 indicated statistical significance. Asthma was defined as parental-reported wheezing in the last 12 months, plus at least one of the following: i) asthma diagnosis ever, ii) wheezing during/after physical exercise in the last 12 months, and iii) sleep interruption due to wheezing in the last 12 months (Pires et al. 2018). Eczema was defined as the presence of an itchy rash at any point during the last 12 months involving the folds of the elbows, behind the knees, in front of the ankles, buttocks, or around the neck, ears or eyes (Singh et al. 2018).

The additional questions part consisted of 21 questions to measure other risk factors that can affect the prevalence and severity of asthma, rhinitis, and eczema symptoms in pre-school children. Parents were asked about having a household smoker, history of asthma or atopy in the first-degree relatives of the child, whether the child was breastfed and some other questions.

#### Data Collection

A list of all government nurseries was obtained from the Education Council. Approval was granted from the Education Council to distribute the questionnaires to be filled in by parents or guardians of the students. Moreover, the questionnaires were also distributed among kindergartens.

# Data Analysis

Data was entered and analysed using SPSS version 20. All questions were coded and then transferred to SPSS for analysis. Descriptive statistical analysis included frequencies for categorical data. We used t-test and chi-square test to compare continuous and categorical variables.

# Ethical Issues

An ethics permission letter to conduct the study was obtained from Ajman University to get the approval of distributing the questionnaires among nurseries and kindergartens. Another ethics permission letter was obtained from the Education Council for distributing the questionnaire among governmental

nurseries. Prior to data collection, a written and signed consent form was obtained from parents or legal guardians, and confidentiality of participants was maintained at all times. Participants were informed that they have the right to withdraw from the study at any time, and they were also informed that their participation is voluntary.

# Results

There was a significant difference in weight and height between boys and girls; boys were significantly taller and lighter than girls (Table 1). Boys had a very high, significant prevalence of wheeze ever than girls. They also had high significant current wheezing and diagnosed asthma than girls, but had significantly lower speech limitation than girls (Table 2).

There was a significant difference in the prevalence of rhinitis symptoms between boys and girls; boys had higher prevalence rates than girls (Table 3). Boys had significantly higher prevalence rates of rashes ever, current rashes, rash locations and eczema ever than girls (Table 4).

**Table 1.** Physical Measurements of All Children

Variable	Boys	(2000)	Girls (2	2000)	All (4000)		
	Mean	S.D	Mean	S.D	Mean	S.D	
Age	3.3	1.4	3.4	1.4	3.3	1.4	
Height	91.6	10.9	92.3***	11.8	92.0	11.3	
Weight	17.7	5.3	16.9***	4.9	17.3	5.2	
BMI	23.5	8.2	23.3	9.2	23.4	9.3	

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

Table 2. Prevalence and Severity of Asthma Symptoms

Symptoms	Boys	s (2000)	Girls	(2000)	All (	4000)
	N	%	N	%	N	%
Wheeze Ever	944	47.2***	654	32.7	1616	40.4
Current Wheezing	906	45.3**	840	42.0	1752	43.8
Wheezing Attacks:						
None	704	35.2	750	37.5	1448	36.2
1-3	786	39.3	666	33.3	1464	36.6
4-12	52	2.6	48	2.4	100	2.5
≥12	36	1.8	14	0.7	12	1.3
Sleep Disturbance:						
None	680	34	560	28	1172	29.3
1-3	880	44.1	820	40.6	1700	42.5
4-12	48	2.4	52	2.6	100	2.5
Once a Week	24	1.2	28	1.4	52	1.3
Speech limitation	720	36.0**	762	38.1	1504	37.6
Diagnosed Asthma	564	28.2**	488	24.4	1060	26.5
Dry Cough	722	36.1	722	36.1	1444	36.1
Exercises- induced Asthma	748	37.4	758	37.9	1504	37.6

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

**Table 3.** Prevalence and Severity of Rhinitis Symptoms

Symptoms	Boy	rs (2000)	Girls	(2000)	All (	(400)
	N	%	N	%	N	%
Rhinitis Ever	864	44.4***	682	39.8	1546	42.2
Current Rhinitis	775	41.1**	663	39.8	1438	40.5
Itchy watery eye	757	40.2**	631	37.9	1388	39.1
Season:						
Summer	333	19.2	261	17.4	594	18.4
Winter	856	49.2	679	45.3	1535	47.5
Spring	140	7.2	151	1.10	291	9.0
Autumn	20	1.2	18	1.2	38	1.2
Effect of Rhinitis on						
Daily Activity						
None	700	40.4	593	39.5	1293	40.0
Little	543	31.3	397	26.5	940	29.1
Moderate	77	4.4	86	5.7	163	5.0
A lot	29	1.7	34	2.3	63	1.9
Hay fever	814	47.0	702	46.8	1516	46.9

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

**Table 4.** Prevalence and Severity of Eczema Symptoms

Symptoms	Boy	s (2000)	Girls	(2000)	All (4	4000)
	N	%	N	%	N	%
Rashes Ever	794	40.7***	632	36.8	1426	38.9
Current Rashes	675	34.6*	501	32.7	1236	33.7
Rashes Locations	570	31.1*	451	28.2	1021	29.8
Age first occurred						
<b>≤</b> 2	723	39.5	641	40.1	1364	39.8
2-4	559	28.7	435	27.2	994	29.0
≥ 5	110	6.0	78	4.9	188	5.5
Cleared rash past 12 month	1028	56.3	830	52.0	1858	54.3
Wake at night						
Never	1351	73.8	1265	79.2	2616	76.3
≤ 1 night per week	415	22.7	284	17.8	699	20.4
1 or more night per week	26.2	1.3	16	1.0	42	1.2
Eczema Ever	1136	60.0**	940	56.3	2076	58.0

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

There was a trend showing higher prevalence of current wheezing, current asthma, incense affecting breathing, perfume affecting breathing among girls compared with boys. Twenty one percent of boys and 27% of girls were exposed to parental smoking (Table 5).

Mean age of onset of asthma for boys and girls was 1.6 years, and mean age for recovery from asthma for boys and girls were 1.8 and 1.7 years, respectively. Both boys and girls had the same mean age of onset for rhinitis which was 1.8

years and the mean age of recovery for boys and girls were the same (1.8, 1.7 years) (Table 6).

The prevalence rates of asthma and asthma symptoms (wheeze ever, current wheezing, number of wheezing attacks, number of sleep disturbances per week, speech limitation, asthma, dry cough and exercise-induced asthma) were significantly higher in children who breastfed less than 10 months compared to those who breastfed more than 10 months (Table 7).

The prevalence rates of rhinitis symptoms (rhinitis ever, current rhinitis, itchy watery eyes, and hay fever) were significantly higher in children who breastfed less than 10 months, compared to those who breastfed more than 10 months (Table 7).

The prevalence rates of eczema symptoms (rash ever, current rash, and eczema) were significantly higher in children who breastfed less than 10 months compared to those who breastfed more than 10 months (Table 7).

Children who were exposed to parental smoking had significantly higher prevalence rates of asthma and respiratory symptoms than unexposed children (Table 8). Children whose parents had history of asthma had more prevalence, and severity of symptoms of asthma compared to those parents who never had asthma. In general, for all symptoms of asthma, the difference was highly significant  $(P \le 0.001)$  (Table 9).

There was a very high significant difference in prevalence of rhinitis symptoms in children who had asthma, compared to children who never had asthma. Children without asthma had a significantly lower prevalence of rhinitis symptoms (Table 10).

There was significant difference in prevalence of eczema symptoms in asthmatic children compared with children without asthma. Children without asthma had significantly less prevalence of eczema symptoms (Table 10).

There was a very high significant difference in prevalence of asthma symptoms in children who had rhinitis compared to children without rhinitis. Children without rhinitis had significantly less prevalence of asthma symptoms. Children with rhinitis had significantly higher prevalence of eczema and rashes than children without rhinitis (Table 11).

Children with eczema had significantly higher prevalence rates of asthma and respiratory symptoms than children without eczema. There was a higher significant difference in prevalence of rhinitis between children with eczema and children without eczema (P≤0.001). Children, who never had eczema, have significantly lower prevalence rates of rhinitis symptoms (Table 12).

 Table 5. Additional Questions

Questions	Boys	(2000)	Girls	(2000)	All (	4000)
	N	%	N	%	N	%
Wheezing now	21	4.7	28	6.0	49	5.3
Asthma now	14	3.1	16	3.4	30	3.3
Treatment for Asthma now	15	3.3	20	4.3	35	3.8
Smoker at home	95	21.1	128	27.2	223	24.2
Incense affect breathing	56	12.4	64	13.6	120	13.0
Perfume affect breathing	30	6.7	39	8.3	69	7.5
Father suffer from asthma	22	4.9	35	7.4	57	6.2
Father suffer from eczema	33	7.3	37	7.9	70	7.6
Mother suffer from asthma	22	4.9	32	6.8	54	5.9
Mother suffer from eczema	33	7.3	45	9.6	78	8.5
Child breast feed	379	84.2	399	84.9	778	84.6
Animal at house	83	18.4	89	18.9	172	18.7
Brothers or Sisters has asthma	47	10.4	49	10.4	96	10.4
Brothers or Sisters has rhinitis	87	19.3	76	16.2	163	17.7
Brothers or Sisters has eczema	82	18.2	102	21.7	184	20.0
Change house recently	65	14.4	70	14.9	135	14.7
Type of housing						
Villa	330	73.3	342	72.8	672	73.0
Apartment	120	26.7	128	27.2	248	27.0
Diet Changed recently	46	10.2	52	11.1	98	10.7
Meals of fruit in week						
Daily	246	54.7	262	55.7	508	55.2
Twice a week	126	28.0	134	28.5	260	28.3
Rarely	68	15.1	71	15.1	139	15.1

**Table 6.** Age of Onset and Recovery of Asthma, Wheezing, Rhinitis, and Eczema (years)

Variable	Boys (2000)		Girls (2000)		All (4000)	
	Means	S.D	Means	S.D	Means	S.D
Age of Asthma Onset	1.56	1.2	1.58	1.4	1.8	1.3
Age of Wheezing Onset	1.54	1.3	1.7	1.3	1.6	1.3
Age of Asthma Recovery	2.13	1.8	1.8	1.7	2.0	1.7
Age of Rhinitis Onset	1.67	1.38	1.75	1.4	1.7	1.4
Age of Rhinitis Recovery	1.56	1.82	2.1	1.79	1.9	1.8
Age of Eczema Onset	1.2	1.2	1.26	1.22	1.2	1.2
Age of Eczema Recovery	1.2	1.4	1.15	1.32	1.2	1.4

**Table 7.** Prevalence and Severity of Asthma, Rhinitis and Eczema in Children who Breastfed Less than and More than 10 Months

Symptom	<b>Children Breastfeed ≤ 10</b>	Children Breastfeed > 10
	Months (n=3249) %	Months (n=751) %
Wheeze Ever	44.0 ***	12.8
Current Wheeze	48.2 ***	9.4
No. of Wheeze Attacks	40.6 ***	7.7
No. of Sleeping	47.7 ***	6.6
Disturbances per week	47.7	0.0
Speech Limitation	41.7 ***	1.5
Asthma Ever	29.5 ***	6.3
Dr Cough	39.2 ***	11.4
Exercise-induced Asthma	42.1 ***	1.7
Rhinitis Ever	45.5 ***	16.6
Current Rhinitis	43.9 ***	14.5
Itchy Watery Eyes	43.3 ***	6.5
Hay Fever	45.3 ***	4.4
Rash Ever	42.8 ***	7.3
Current Rash	37.1 ***	6.8
Eczema Ever	63.6 ***	17.1

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

**Table 8.** The Effect of Parental Smoking on Prevalence and Severity of Asthma Symptoms

Symptoms	Exposed (n=20		Not Exposed Children (n=1599)		
	N	%	N	%	
Wheezing Ever	1015	50.9***	426	26.7	
Current Wheezing	1092	52.9***	507	31.8	
Wheezing Attacks:					
None	774	43.3***	441	28.0	
1-3	771	43.1***	455	29.1	
4-12	40	2.2	45	2.9	
≥12	35	2.0***	9	0.6	
Sleep Disturbance:					
None	576	33.8***	262	24.0	
1-3	896	52.6***	471	31.2	
4-12	45	2.6***	35	2.3	
Once a Week	17	1.0***	25	1.7	
Speech limitation	924	46.1***	384	24.9	
Diagnosed Asthma	533	31.4***	311	20.7	
Dry Cough	908	43.9***	413	25.9	
Exercises induced Asthma	963	46.6***	414	26.0	

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

Table 9. Effect of Parental History of Asthma on Symptoms of Asthma

Symptoms	Father with Asthma		Fa wit	without Mother with  Asthma		without Mother w				ther nout hma
	N	%	N	%	N	%	N	%		
Wheezing Ever	1162	50.5***	318	23.4	888	54.6***	593	29.2		
Current Wheezing	1246	54.2***	353	26.0	967	59.5***	633	31.1		
Wheezing Attacks:										
None	957	47.4***	256	19.3	636	47.4***	579	28.8		
1-3	932	40.5***	296	22.2	602	44.8***	623	31.0		
4-12	49	2.4***	34	2.6	50	3.7***	35	1.7		
≥12	28	1.2***	14	1.1	26	1.9***	1	0.1		
Sleep Disturbance:										
None	675	35.7***	267	20.2	493	4.7***	447	22.4		
1-3	1103	58.4***	262	20.0	613	50.6	756	37.6		
4-12	36	1.9***	39	19.9	52	4.3***	28	1.4		
Once a Week	22	1.2***	20	1.5	24	2.0***	2	0.9		
Speech limitation	1085	49.4***	226	16.8	887	58.6***	425	20.9		
Diagnosed Asthma	605	32.2***	241	18.3	622	51.7***	224	11.2		
Dry Cough	1019	44.3***	303	22.3	787	48.4***	533	26.2		
Exercises induced Asthma	1136	49.3***	242	17.8	861	52.9***	515	25.3		

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

**Table 10.** Comparing Rhinitis and Eczema Symptoms between Children with Asthma and Children without Asthma

Symptoms	Children	with Asthma		n without thma
	N	%	N	%
Rhinitis Ever	371	44.0***	806	34.2
Current Rhinitis-	415	49.3***	722	31.0
Itchy watery eye	389	46.4***	698	30.0
Rhinitis Season:				
Summer	200	23.8***	394	17.1
Winter	506	60.2***	1016	44.2
Spring	68	8.1***	151	6.6
Autumn	7	0.8***	23	1.0
Rhinitis Affect Daily Activity				
None	390	46.4***	860	37.4
Little	320	38.0***	585	25.4
Moderate	53	6.3***	96	4.2
A lot	18	2.1***	44	1.9
Hay fever	509	60.5***	1001	43.6
Rashes Ever	366	43.2***	739	31.3
Current Rashes	331	39.0***	682	28.9
Rashes Locations	342	40.3***	675	29.3

Eczema Age First Occurred				
≤2 years				
2-4 years	389	45.9*	853	37.0
≥ 4 years	316	37.3*	593	25.7
Cleared rash past 12 mo Rash	53	6.3*	69	3.0
Wake at night	586	69.4***	1183	51.3
Never				
≤ 1 night per week	570	67.2**	1837	79.6
1 or more night per week	233	27.5**	402	17.4
Eczema Ever	1	1.1**	2	0.2
	603	71.4***	1347	57.1

**Table 11.** Comparing Asthma and Eczema Symptoms between Children with Rhinitis and Children without Rhinitis

Symptoms	Children V	Vith Rhinitis		n Without ainitis
	N	%	N	%
Wheezing Ever	818	52.9***	658	31.1
Current Wheezing	902	58.3***	698	33.0
Wheezing Attacks:				
None	555	43.5***	657	31.7
1-3	547	42.9***	679	32.7
4-12	44	3.4***	41	2.0
≥12	36	2.8***	8	0.4
Sleep Disturbance:				
None	410	34.8***	528	26
1-3	609	51.7***	758	37.3
4-12	49	4.2***	31	1.5
Once a Week	16	1.4***	26	1.3
Speech limitation	741	50.4***	568	27.4
Diagnosed Asthma	371	31.5***	473	23.4
Dry Cough	751	48.6***	568	26.9
Exercises induced Asthma	771	49.9***	604	28.6
Rashes Ever	849	54.9***	577	27.3
Current Rashes	691	44.7***	545	25.8
Rashes Locations	508	37.4***	511	24.7
Age first occurred				
≤2	575	42.3***	789	38.2
2-4	524	33.9***	466	22.6
≥5	111	7.2***	77	3.7
Cleared rash past 12 month	1040	76.5***	818	39.6
Wake at night				
Never	891	65.6*	1723	83.4
≤ 1 night per week	397	29.2*	302	14.6
1 or more night per week	2	1.4*	6	0.8
Eczema Ever	1143	77.2***	933	44.8

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

**Table 12.** Comparing Asthma and Rhinitis Symptoms between Children with Eczema and Children without Eczema

Symptoms	Children V	Vith Eczema	Children Without Eczema		
	N	%	N	%	
Wheezing Ever	895	43.1*	484	32.5	
Current Wheezing	959	46.2**	544	36.6	
Wheezing Attacks:					
None	853	43.1***	262	20.6	
1-3	929	46.9***	297	23.3	
4-12	44	2.2	41	2.8	
≥12	35	1.8	9	0.6	
Sleep Disturbance:					
None	677	34.7	251	20.0	
1-3	1089	55.8	278	22.2	
4-12	49	2.5	31	2.5	
Once a Week	16	0.8	26	2.1	
Speech limitation	872	42.4***	427	28.9	
Diagnosed Asthma	603	30.9***	241	19.2	
Dry Cough	779	37.5***	443	29.8	
Exercises induced Asthma	846	40.8***	432	29.1	
Rhinitis Ever	1143	55.1***	337	22.7	
Current Rhinitis	883	43.5***	543	36.6	
Itchy watery eye	884	43.5***	494	33.3	
Season:					
Summer	409	21.3***	183	14.3	
Winter	1192	62.0***	340	26.6	
Spring	186	9.7***	80	6.3	
Autumn	22	1.1***	11	0.9	
Affect Daily Activity					
None	991	51.6***	283	22.2	
Little	691	36.0***	236	18.5	
Moderate	92	4.8***	68	5.3	
A lot	35	1.8***	28	2.2	
Hay fever	1153	60.0***	363	28.5	

<sup>\*:</sup>  $P \le 0.05$ ; \*\*:  $P \le 0.01$ ; \*\*\*:  $P \le 0.001$ 

Boys had higher prevalence rates of asthma, eczema, rhinitis, asthma and eczema, asthma and rhinitis, eczema and rhinitis and asthma, rhinitis and eczema than girls (Table 13). The prevalence rates of asthma, rhinitis and eczema was higher in children who breastfed less than 10 months compared with those who breastfed more than 10 months (Table 14).

**Table 13.** Prevalence of Asthma, Rhinitis, Eczema Symptoms in Boys (2,000), Girls (2,000) and All (4,000)

Boys (1950)	Asthma Only	Eczema Only	Rhinitis Only	Asthma & Eczema Only	Asthma & Rhinitis Only	Eczema & Rhinitis Only	Asthma & Rhinitis & Eczema
	24.9%	58.2%	44.3%	17.8%	12.0%	34.0%	11.2%
Girls (1718)	Asthma Only	Eczema Only	Rhinitis Only	Asthma & Eczema Only	Asthma & Rhinitis Only	Eczema & Rhinitis Only	Asthma & Rhinitis & Eczema
	21.1%	54.7%	39.7%	14.9%	8.0%	27.9%	7.5%
All Children (3668)	Asthma Only	Eczema Only	Rhinitis Only	Asthma & Eczema Only	Asthma & Rhinitis Only	Eczema & Rhinitis Only	Asthma & Rhinitis & Eczema
	23.1%	56.6%	42.1%	16.4%	10.1%	31.2%	9.5%

**Table 14.** Prevalence and Severity of Asthma, Rhinitis, and Eczema Symptoms in Children who Breastfeed  $\leq 10$  Months and > 10 Months

Breastfeed ≤ 10 Months (n=3249)	Asthma Only	Eczema Only	Rhinitis Only	Asthma & Eczema Only	Asthma & Rhinitis Only	Eczema & Rhinitis Only	Asthma & Rhinitis & Eczema
(II-3249)	6.3%	18.7%	2.4	7.9%	0.5%	20.6%	10.5%
Breastfeed > 10 Months	Asthma Only	Eczema Only	Rhinitis Only	Asthma & Eczema Only	Asthma & Rhinitis Only	Eczema & Rhinitis Only	Asthma & Rhinitis & Eczema
>10				& Eczema	& Rhinitis	& Rhinitis	& Rhinitis &

# **Discussion**

Previous studies have identified genetic, environmental, behavioral, and socioeconomic factors associated with the development of allergic diseases in childhood, likely to reflect complex interactions between genes and environmental exposures (Lambercht and Hammad 2017).

In the present study, current prevalence and severity of asthma, rhinitis and eczema among pre-school children in Dubai, Sharjah, Al-Ain and Abu Dhabi (UAE) were reported and analysed. The global prevalence of asthma among 6- to 7-year-old and 13- to 14-year-old children were estimated at 14.1% and 11.7%, respectively in 2002 (Grize et al. 2006). We can speculate that asthma prevalence among different age groups that are presently growing linearly will level at a plateau level, as has happened in other countries (Qu et al. 2013, Yangzong et al. 2012, Dong et al. 2012, Hong et al. 2012), or will be in the region of steep increase in a sigmoid curve as in Beijing (Pearce et al. 2007).

The present study, with a relatively large sample size, shows significantly high prevalence of asthma, asthmatic symptoms, rhinitis and eczema. The strength of the upward asthma prevalence trend over the past years is real in spite of the methodological differences amongst various studies. The present study reports more actual prevalence rates, whereas earlier reports may have underestimated prevalence rates.

Studies in Chinese pre-school children found significantly higher asthma in urban areas than in suburban areas, consistent with other studies (Zhao et al. 2010, Bjerg et al. 2010, Choi et al. 2014). Also, other Chinese studies have found significantly higher asthma prevalence rates in boys than girls, consistent with many Chinese (Zhao et al. 2010, Choi et al. 2014, Postma 2007) and international (Yangzong et al. 2012, Dong et al. 2012, Hong et al. 2012, Almqvist et al. 2008, Zhang et al. 2013) studies. Young boys had a higher asthma prevalence than girls at least until age 13-14 (Weschler 2009), or adolescence (Guarnieri and Balmes 2014, Mi et al. 2006). The time-trend of childhood asthma among 3- to 7-year-old children is most likely well-characterised. The present study represents a comprehensive description of asthma, allergy, and airway symptoms or diseases in pre-school children in the UAE. It also provides a good reference for national or international studies, and comparisons of childhood health issues which will be useful for future similar studies in rapidly developing cities, countries, or regions.

Furthermore, given the parallel exponential uptrends of prevalence rates of childhood asthma in different age groups and of various indicators of rapid modernization in the UAE, we can ask whether the disease increase is associated with changes in environmental exposures (indoor and outdoor) and family lifestyles that have occurred with rapid modernization. Many studies have found significant associations between air pollution and childhood asthma and other respiratory diseases and/or symptoms (Asher et al. 1995). However, the annual average concentrations of typical outdoor air pollutants in the Gulf region have trended down. Thus, it is possible that environmental exposures whose sources are indoors rather than outdoors may have stronger associations with childhood asthma than outdoor air pollution (Li et al. 2011, Asher et al. 1995, Qian et al. 2011, Bornehag et al. 2004, Dong et al. 2008, Liu et al. 2014, Hu et al. 2014).

It has been previously reported that some environmental factors, including pet-keeping, indoor tobacco smoking, using wood as cooking fuel, living within 200m of a highway or busy road, and home dampness-related indicators, have positive and significant associations with childhood asthma and other diseases or symptoms.

Attention should be given to the health effects of changing environmental exposures with indoor sources due to newly-fashioned lifestyles that have developed as the economy in many countries has grown.

- 1. Prevalence and severity of symptoms of asthma, allergic rhinitis, and eczema: first of all, as for the prevalence and severity of asthma symptoms in all children, we found that the prevalence rates of symptoms of wheezing ever, current wheezing, dry cough, speech limitation, and exercise-induced asthma were high. There was significant difference in asthma, rhinitis and eczema symptoms between boys and girls.
- 2. Effect of breast-feeding, passive smoking and parental history on prevalence and severity of symptoms of asthma, allergic rhinitis, and eczema.

## **Breastfeeding**

Although prolonged breastfeeding was shown to reduce the risk of allergic and respiratory disease, still the fact that breastfeeding can prevent allergic disease remains controversial, as there are no reports from developing countries that support this issue. In this study, we tried to assess the relationship between breastfeeding and the development of childhood asthma and allergic diseases. We found that there was significant difference in the prevalence of asthma for children who breastfeed more than 10 months compared to children who breastfeed less than 10 months (P≤0.001). Breastfeeding may be confounded by other factors such as income.

#### Passive Smoking

Worldwide, smoking rates are increasing despite all of the campaigns to eliminate smoking and hinder the detrimental effects of passive smoking. Children who were exposed to passive smoking, either in utero or during their adulthood, may have an increased prevalence of allergies and asthma. In the present study, it has been found that children who are exposed to parental smoking have significantly higher prevalence rates of asthma symptoms ( $P \le 0.001$ ). Smoking may be confounded by other factors such as income.

Boys had higher prevalence rates of asthma, eczema, rhinitis, asthma and eczema, asthma and rhinitis, eczema and rhinitis and asthma, rhinitis and eczema than girls (Table 13). The prevalence rates of asthma, rhinitis and eczema was higher in children who breastfed less than 10 months compared with those who breastfed more than 10 months (Table 14).

# Parental History

Although hereditary factors have an important role in asthma and in other allergic diseases, the mechanisms underlying the inheritance of these disorders are still poorly understood. We investigated the effect of parental history on the prevalence and severity of asthma and we found that children, whose parents had

history of asthma, had more prevalence and severity of symptoms of asthma compared to those children whose parents never had asthma. The difference was very highly significant ( $P \le 0.001$ ).

As breastfeeding has a protective effect in relation to early asthma, it should be encouraged. As passive smoking has significant effect on prevalence and severity of asthma, it should be discouraged. We need to provide effective awareness programmes for parents about asthmatic patients, all allergic diseases, and towards avoiding certain triggers of asthma.

#### Conclusion

The present study has provided an up-to-date description of the prevalence and severity of asthma, rhinitis and eczema in pre-school children in the UAE. In this study, data has illustrated that there is a significant difference of the prevalence and severity of symptoms of asthma and allergic rhinitis between boys and girls. However, girls showed lower prevalence of asthma, wheezing, rhinitis and eczema compared to boys.

In addition, results have demonstrated that factors such as beast-feeding, passive smoking and parental history have an important effect on the prevalence and severity of symptoms of asthma, allergic rhinitis and eczema. The data are based on self-reported data. The healthcare organization in UAE has to encourage campaigns that are encouraging breast-feeding and discouraging smoking. Additionally, there is a need for asthma education programmes towards avoiding certain triggers of asthma and allergic diseases. The present study can be used as a baseline study to implement asthma and allergy intervention programmes in children.

# Limitations

In the present study, we have used the ISAAC questionnaire which has been designed for 6- to 7-year-old and 13- to 14-year-old children because we do not have a specific questionnaire for pre-school children.

#### Acknowledgments

The authors would like to thank the Educational Authorities, nurseries, kindergartens for approving the study, and parents of children who have participated in the study.

# References

- Aït-Khaled N, Pearce N, Anderson HR, Ellwood P, Montefort S, Shah J, et al. (2009) Global map of the prevalence of symptoms of rhinoconjunctivitis in children: the international study of asthma and allergies in childhood (ISAAC) phase three. *Allergy* 64(1): 123–148.
- Al Ghobain MO, Al-Hajjaj MS, Al Moamary MS (2012) Asthma prevalence among 16-to 18-year-old adolescents in Saudi Arabia using the ISAAC questionnaire. *BMC Public Health* 12(239): 1–5.
- Almqvist C, Worm M, Leynaert B (2008) Impact of gender on asthma in childhood and adolescence: a GALEN review. *Allergy* 63(1): 47–57.
- Asher MI, Keil U, Anderson HR (1995) International study of asthma and allergies in childhood (ISAAC): rationale and methods. *European Respiratory Journal* 8(24): 483–491.
- Asher MI, Montefort S, and Björkstén B (2006) Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. *The Lancet* 368(9537): 733–743.
- Barnes PJ (2012) Asthma. In *Harrison's Principles of Internal Medicine*, Chapter 281: (Pt 18): 2012–2115.
- Barreto ML, Cunha SS, Alcantara-Neves N, Carvalho LP, Cruza A, Stein RT, et al. (2006) Risk factors and immunological pathways for asthma and other allergic diseases in children: background and methodology of a longitudinal study in a large urban center in Northeastern Brazil (Salvador-SCAALA study). *BMC Pulmonary Medicine* 6(15): 1–10.
- Barreto ML, Cunha SS, Fiaccone R, Esquivel R, Amorim LD, Alvim S, et al. (2010) Poverty, dirt, infections and non-atopic wheezing in children from a Brazilian urban center. *Respiratory Research* 11(1): 167.
- Bateman ED, Zar HJ, Hurd SS (2008) Global strategy for asthma management and prevention: GINA executive summary. *European Respiratory Journal* 31(1): 143–178.
- Bauer GE, Hull RD, Stokes GS (1973) The reversibility of side effects of guanethidine therapy. *Medical Journal of Australia* 1(19): 930–933.
- Beasley R (1998) Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *The Lancet* 351: 1225–1232.
- Bjerg A, Sandström T, Lundbäck B (2010) Time trends in asthma and wheeze in Swedish children 1996-2006: prevalence and risk factors by sex. *Allergy* 39(1): 48–55.
- Bornehag CG, Sundell J, Sigsgaard T (2004) Dampness in buildings and health (DBH): Report from an ongoing epidemiological investigation on the association between indoor environmental factors and health effects among children in Sweden. *Indoor Air* 14(Suppl. 7): 59–66.
- Bosnic-Anticevich S, Smith P, Abramson M, Hespe CM, Johnson M, Stosic R, et al. (2020) Impact of allergic rhinitis on the day-to-day lives of children: insights from an Australian cross-sectional study. *BMJ Open* 10(11): 1–12.
- Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Canonica GW, et al. (2020) Allergic rhinitis. *Nature Reviews: Disease Primers* 6(Dec): 96.
- Burr M.L, Emberlin JC, Treu R (2003) Pollen counts in relation to the prevalence of allergic rhinoconjunctivitis, asthma and atopic eczema in the International Study of Asthma and Allergies in Childhood. *Clinical and Experimental Allergy* 33(12): 1675–1680.

- Cauwenberge PV (2003) Allergic rhinitis, ARIA guidelines and antihistamines: state of the art, Blackwell Publishing, Oxford, 2005. (ISAAC). *Clinical and Experimental Allergy* 33(12): 1675–1680.
- Choi J, Chun C, Sun Y (2014) Associations between building characteristics and children's allergic symptoms-a cross-sectional study on child's health and home in Seoul, South Korea. *Built Environment* 75(May): 176–181.
- Ciprandi G, Vizzaccaro A, Cirillo I, Crimi P, Canonica DW (1996) Increase of Asthma and Allergic Rhinitis Prevalence in Young Italian Men. *International Archives of Allergy and Immunology* 111(3): 278–283.
- Cohen S, Dworetzky M, Frick OL (2003) Coca and Cooke on the classification of hypersensitiveness. *Journal of Allergy and Clinical Immunology* 111(1): 205–210.
- Dong GH, Ma YN, Ding HL (2008) Effects of housing characteristics and home environmental factors on respiratory symptoms of 10,784 elementary school children from northeast China. *Respiration* 76(1): 82–91.
- Dong W, Zhou Y, Su W (2012) Relationship of multiple risk factors in infancy with 26 asthma morbidity at age 7 to 8 years in suburb and urban of Shanghai (in Chinese). *Journal of Clinical Pediatrics* 30(12): 1139–1143.
- Duggan EM, Sturle J, Fitzgerald AP, Perry IJ, Hourihan JOB (2012) The 2002-2007 trends of prevalence of asthma, allergic rhinitis and eczema in Irish schoolchildren. *Pediatric Allergy and Immunology* 23(5): 464–471.
- Ellegard K, Karlsson G (1994) Nasal congestion during the menstrual cycle. *Clinical Otolaryngology and Allied Sciences* 19(5): 400–403.
- Ellegard E, Karlsson G (1999) Nasal congestion during pregnancy. *Clinical Otolaryngology and Allied Sciences* 24(4): 307–311.
- Forno E, Gogna M, Cepeda A, Yañez A, Sole´D, Cooper P, et al. (2015) Asthma in Latin America. *Thorax* 70(9): 898–905.
- Gaga M, Zervas E, Grivas S, Castro M, Chanez P (2007) Evaluation and management of severe asthma. *Current Medicinal Chemistry* 14(9): 1049–1059.
- Godfrey S (1996) Bronchiolitis and asthma in infancy and early childhood. *Thorax Supplement* (2): 360–369.
- Girgis, I. H., Yassin, A., Hamdy, H., Moris M (2007) Estimation of effect of drugs on the nasal circulation. *The Journal of Laryngology and Otology* 88(12): 1163–1168.
- Graf P (1997) Rbtis Medicamentosa: aspects of pathophysiology and treatment. *Allergy* 52(5): 28–34.
- Gregory C, Cifaldi M, and Tanner LA (1999) Targeted intervention programs: creating a customized practice model to improve the treatment of allergic rhinitis in a managed care population. *American Journal of Managed Care* 5(43): 485–496.
- Grize L, Gassner M, Wüthrich B, B Bringolf-Isler B, Takken-Sahli K, Sennhauseetr FH et al. (2006) Trends in prevalence of asthma, allergic rhinitis and atopic dermatitis in 5-7-year old Swiss children from 1992 to 2001. *Allergy* 61(5): 556–562.
- Guarnieri M and Balmes RJ (2014) Outdoor air pollution and asthma. *The Lancet* 383(9928): 1581–1592.
- Gwaltney JM (1996) Acute community-acquired sinusitis. *Clinical Infectious Diseases* 23(6): 1209–1223.
- Gwaltney JM, Scheld WM, Sande MA, Sydnor A (1992) The microbial etiology and antimicrobial therapy of adults with acute community-acquired sinusitis: a fifteen-year experience at the University of Virginia and review of other selected studies. *Journal of Allergy and Clinical Immunology* 90(3): 457–461.
- Hong S, Son DK, Lim WR, Kim SH, Kim H, Yumet HY, et al. (2012) The prevalence of atopic dermatitis, asthma, and allergic rhinitis and the comorbidity of allergic diseases in children. *Environmental Health Toxicology* 27: 1–8.

- Hu Y, Liu W, Huang C, Zou ZJ, Zhao ZH, Shen L, et al. (2014) Home dampness, childhood asthma, hay fever, and airway symptoms in Shanghai, China: associations, dose-response relationships, and lifestyle's influences. *Indoor Air* 24(5): 450–463.
- Kaufman HS (1986) Timolol-induced vasomotor rhinitis: a new iatrogenic syndrome. *Archives of Ophthalmology* 104(Pt7): 967–970.
- Krol A, Krafchik B (2006) The differential diagnosis of atopic dermatitis in childhood. *Dermatologic Therapy* 19(2): 73–82.
- Lambrecht BN and Hammad H (2017) The immunology of the allergy epidemic and the hygiene hypothesis. *Nature Immunology* 18(10): 1076–1083.
- Lau S, Nickell R, Niggemann B, Gruber C, Summerfield C, Illi S et al. (2002) The development of childhood asthma: lessons from the German Multicentre Allergy Study (MAS). *Paediatric Respiratory* Reviews 3(3): 265–272.
- Li F, Zhou Y, Li S, Xingming FJ, Jin X, Yan C, et al. (2011) Prevalence and risk factors of childhood allergic diseases in eight metropolitan cities in China: a multicenter study. *BMC Public Health* 11(1): 437–445.
- Liu W, Huang C, Hu Y, Sundell J, Zou Z, Zhao Z (2014) Association of building characteristics, residential heating and ventilation with asthmatic symptoms of preschool children in Shanghai: A cross-sectional study. *Indoor Built Environment* 23(2): 270–283
- Mallol J, Crane J, Von Mutius E, Odhiambo J, Keil U, Stewart A (2013) The international study of asthma and allergies in childhood (ISAAC) phase three: a global synthesis.; ISAAC phase three study group. *Allergologia et Immunopathologia* 41(2): 73–85.
- Malone DC, Lawson KA, Smith DH, Arrighi HM, Battista C (1997) A cost of illness study of allergic rhinitis in the United States. *The Journal of Allergy and Clinical Immunology* 99(1): 22–27.
- Mi YH, Norbäck D, Tao J, Mi YL, Ferm M (2006) Current asthma and respiratory symptoms among pupils in Shanghai, China: influence of building ventilation, nitrogen dioxide, ozone, and formaldehyde in classrooms. *Indoor Air* 16(6): 454–464.
- Moss RB (1989) Allergic etiology and immunology of asthma. *Annuals of Allergy* 63(6): 566-77.
- Myers, TR (2012) Severe acute asthma: an attempt to identify the quiet before the storm. *Respiratory Care* 57(9): 1526–1527.
- Nutten S (2015) Atopic dermatitis: global epidemiology and risk factors. *Annual Nutrition and Metabolism* 66(Suppl. 1): 8–16.
- Okamoto Y, Sakurai D, Horiguchi S (2004) Allergic rhinitis in children: environmental factors. *Clinical Experimental Allergy Review* Clinical 4(1): 9–14.
- Pearce N, Aït-Khaled N, Beasley R, Mallol J, Keil U, Mitchell Ed et al. (2007) Worldwide trends in the prevalence of asthma symptoms: phase iii of the international study of asthma and allergies in childhood (ISAAC). *Thorax* 62(9): 758–766.
- Pires A de O, Queiroz G de A, de Jesus Silva M, da Silva RR, da Silva HBF, Carneiro NVQ, et al. (2018) Polymorphisms in the DAD1 and OXA1L genes are associated with asthma and atopy in a South American population. *Molecular Immunology* 101(Jul): 294–302.
- Postma DS (2007) Gender differences in asthma development and progression. *Gender Medicine* 4(Suppl. B): S133–S146.
- Poulos LM, Toelle BG, Marks GB (2005) The burden of asthma in children: an Australian perspective. *Pediatric Respiratory Reviews* 6(1): 20–27.
- Proud D, Naclerio RM, Gwaltney JM, Hendley JO (1990) Kinins are generated in nasal secretions during natural rhinovirus colds. *Journal of Infectious Diseases* 161(1): 120–123.

- Qian JJ, Ma JY, Zhou M (2011) A survey on epidemiology and risk factors of bronchial asthma in Baoshan district of Shanghai (in Chinese). *Journal of International Medical Con Pract* 6(Pt 2): 121–124.
- Qu F, Weschler LB, Sundell J, Zhang YP (2013) Increasing prevalence of asthma and allergy in Beijing preschool children: is exclusive breastfeeding for more than 6 months protective? *Chinese Science Bulletin* 58(34): 4190–4202.
- Renzoni E, Forastiere F, Biggeri A, Viegi G, Bisanti L, Chellini E, et al. (1999) Differences in parental- and self-report of asthma, rhinitis and eczema among Italian adolescents. *European Respiratory Journal* 14(3): 597–604.
- Robinson RG, Singh AM (2012) Chapter 11: the infant and toddler with wheezing. In *Allergy Asthma Proceeding*, Supplement 1: 36–38.
- Rosser FJ, Forno E, Cooper PJ, Celedo JC (2014) Asthma in Hispanics. An 8-year update. *American Journal* of Respiratory and Critical Care Medicine 189(11): 1316–1327.
- Schiffman SS (1992) Effect of environmental pollutants on taste and smell. Head and neck surgery. *Journal of American Academy of Otolaryngology* 106(6): 693–700.
- Sibbald B (1993) Epidemiology of allergic rhinitis. *Monographs in Allergy* 31: 61.
- Simons FER (1996). Learning impairment and allergic rhinitis. *Allergy and Asthma Proceedings* 17(4): 185–189.
- Singh S, Sharma BB, Salvi S, Chatwal J, Jain KC, Kumar L, et al. (2018) Allergic rhinitis, rhinoconjunctivitis, and eczema: prevalence and associated factors in children. *Clinical Respiratory Journal* 12(2): 547–556.
- Stewart AW, Mitchell EA, Pearce N, Strachan DP, Weiland SK (2001) ISAAC Steering Committee. International study for asthma and allergy in childhood. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic disease in children (ISAAC). *International Journal of Epidemiology* 30(1): 173–179.
- Strina A, Barreto ML, Cooper PJ, Rodrigues LC (2014) Risk factors for non-atopic asthma/ wheeze in children and adolescents: a systematic review. *Emerging Themes in Epidemiology* 11(1): 5.
- Swartz A, Collier T, Young CA, Cruz E, Bekmezian A, Coffman J, et al. (2019) The effect of early child care attendance on childhood asthma and wheezing: a meta-analysis. *Journal of Asthma* 56(3): 252–262.
- Teng NT, Shek LP, Goh DYT, Chew FT, Bee WL (2006) Prevalence of asthma and comorbid allergy symptoms in singaporean preschooler. *Asian Pacific Journal of Allergy and Immunology* 24(4): 175–182.
- Tootoonchi P (2004) Prevalence of Asthma, related symptoms and risk factors in children younger than 5 years. Tehran: Department of Social Medicine, School of Medicine, University of Medical Sciences.
- Von Kobyletzki LB, Bornehag C, Hasselgren M, Larsson M, Lindström CB, Svensson A (2012) Eczema in early childhood is strongly associated with the development of asthma 16 and rhinitis in a prospective cohort. *BMC* 12(1): 11.
- Von Mutius E, Pearce N, Beasley R, Cheng S, Von Ehrenstein O, Björkstén B, et al. (2000) International patterns of tuberculosis and the prevalence of symptoms of asthma, rhinitis, and eczema. *Thorax* 55(6): 449–453.
- Wahn U, Von Mutius E (2001) Childhood risk factors for atopy and the importance of early intervention. *Journal of Allergy and Clinical Immunology* 107(4): 567–574.
- Weiland SK, Von Mutius E, Husing A, Asher MI (1999) Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe. *The Lancet* 353(Pt 9169): 2040–2041.

- Weiland SK, Husing A, Strachan DP, Rzehak P, Pearce N (2004) Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. *Occupational and Environmental Medicine* 61(7): 609–615.
- Weinmayr G, Forastiere F, Weiland SK, Rzehak P, Abramidze T, Annesi-Maesano I, et al. (2008) International variation in prevalence of rhinitis and its relationship with sensitisation to perennial and seasonal allergens. *European Respiratory Journal* 32(5): 1250–1261.
- Weschler CJ (2009) Changes in indoor pollutants since the 1950s. *Atmospheric Environment* 43(1): 153–169.
- Yangzong Y, Shi Z, Nafstad ZS, Håheim LL, Luobu O, Bjertness E (2012) The prevalence of childhood asthma in China: a systematic review. *BMC Public Health* 12(1): 860–869.
- Zhang Y, Mo JH, Weschler CJ (2013) Reducing health risks from indoor exposures in rapidly developing urban China. *Environmental Health Perspectives* 121(7): 751–755.
- Zhao J1, Bai J, Shen K, Xiang L, Huang S, Chenet A, et al. (2010) Self-reported prevalence of childhood allergic diseases in three cities of China: a multicenter study. *BMC Public Health* 10(1): 551–557.
- Zollner IK, Weiland SK, Piechotowski I, Gabrio T, Von Mutius E, Link B, et al. (2005) No increase in the prevalence of asthma, allergies, and atopic sensitization among children in Germany: 1992-2001. *Thorax* 60(7): 545–548.