



STUDY ON RISK FACTORS OF CHILDHOOD ASTHMA IN KARACHI, PAKISTAN

Ibne Amin^{1*}, CHU ZhongXia², Iftikhar Ullah³, Ikram Ul Haq⁴ and Irfan Ali⁵

¹*School of Clinical Medicine, Inner Mongolia University for the Nationalities, 536 West Huo Lin He Street, Horqin District, Tongliao City, Inner Mongolia, P.R China*

²*Department of Pediatrics, Affiliated Hospital of Inner Mongolia University for the Nationalities, 1742 Huo Lin He Street, Horqin District, Tongliao City, Inner Mongolia, P.R China*

³*Xian Jiaotong Medical University, 28 Xianning W Road, Jiaoda Commerce Block, Beilin, Xian, Shaanxi, P.R China*

⁴*School of Clinical Medicine, Inner Mongolia University for the Nationalities, 536 West Huo Lin He Street, Horqin District, Tongliao City, Inner Mongolia P.R China*

⁵*Xian Jiaotong Medical University, 28 Xianning W Road, Jiaoda Commerce Block, Beilin, Xian, Shaanxi, P.R China*

ABSTRACT

Purpose: The purpose of this study is to investigate risk factors of childhood asthma in Karachi, Pakistan.

Objective: To determine the risk factor involved in the development of childhood asthma in Karachi, Pakistan.

Materials and methods: This clinical-based study was conducted at the Agha Khan University affiliated Hospital in Karachi from November 2020 to November 2021. The participants were 500 children of age 2 months to 12 years who attended the pediatrics Department of Agha Khan University Hospital in Karachi. Children were divided into two groups based on observations and clinical record, one group of asthmatic patients consist of 250 participants while the second group which was control group also contain 250 non-asthmatic patients and all 500 children were residents of Karachi and nearby urban areas of Pakistan.

Inclusion criteria: Children with good compliance between the ages of 2 months to 12 years who met the diagnostic criteria for bronchial asthma in children were part of the study.

Exclusion criteria: Children with primary or secondary immunodeficiency, combine with other serious diseases such as liver and kidney failure, and arrhythmia. Children who had throat infections, pulmonary tuberculosis, bronchial pneumonia, congenital heart disease, were not included in this study.

Results: Patients had a history of allergies (OR= 3.51, 95% CI= 2.67-4.78), and asthma (OR= 4.6, 95% CI= 2.51-5.62, P<0.05) were strongly associated with the development of asthma in childhood. From the environmental factors passive smoking had great contribution to develop childhood asthma (OR= 3.14, 95%CI= (2.21-4.42)), new house renovation (OR= 1.45, 95%CI=1.31-1.69), weather changes (OR= 0.21, 95% CI= 0.61-0.89), and pet

feeding history (OR= 1.14, 95% CI= 0.73-1.75), also had significant association with childhood asthma. Modestly association was found with obesity (OR=0.09, 95%CI= 0.21-1.02), and cesarean section (OR= 0.25, 95% CI= 0.10-1.49). Breast feeding (OR= 0.64, 95% CI= 0.35-0.39) had no association with asthma while premature delivery (OR=2.90, 95%CI=1.09-3.02) low birth weight (OR=2.61, 95%CI=2.31-2.62) and early exposure to antibiotic in infant and young children (OR=1.46, 95%CI= 1.46-2.99) had significant association. Family history had a mean value 149.5 ± 0.59 with p-value <0.001 that means a patient with a family history of asthma were greater, similarly environmental factor was found more common in asthma patients 135.5 ± 0.78 . Self-factor (123.6 ± 0.77) and pregnancy factor (93 ± 0.65) had significant impact $p=<0.05$.

Conclusion: Eventually, family history, environmental factor, self-factor was found the root cause of childhood asthma in this study, while overall pregnancy modestly had contribution in childhood asthma. Among the pregnancy factor, breastfeeding had a non-significant impact on the development of asthma in childhood

Key words: childhood asthma, risk factors, family history, environmental factors, pregnancy factors

INTRODUCTION

Asthma is a heterogeneous chronic inflammatory disease with reversible bronchoconstriction and arising from the interaction of multiple factors. According to an estimation in 2018, globally 339 million people had suffered from asthma.¹⁶ Asthma emerged as a worse respiratory disorder among children, in 2016 approximately 6.1 million children of age less than eighteen years are suffered from asthma and more than half of these were reported in the United states.¹⁷ However, the mortality rate is higher in adults than children that can be overcome through proper management and care. Gradually, an increase in the prevalence of childhood asthma was found in developed countries including U.K., Germany, Canada, and Australia. Although underdeveloped countries are less likely to face this issue as compared to developed countries.¹⁸ According to a survey its prevalence among the Chinese children of 0-14 years has been raised 2 times that of 1990(1.00%). Asthma exhibited a broad spectrum of potential multiple factors originated from genetics, environmental factors, and lifestyle. Globally, increased incidence cannot merely cause by genetic factors alone, as genetic changes are time taking process to express in generations. Evidence has to present that environmental factors, lifestyle are key events for the increasing trend of childhood asthma.²⁰ Interestingly, in the last two decades it has been reported that asthma can be associated with exposure to new household products, although inconsistency was found in these findings.²² Literature review indicated that early life exposure to household decoration can be linked with allergy and respiratory disorder.²¹

The purpose of this study is to investigate the risk factors of childhood asthma in Karachi, Pakistan. We will assess the pathogenic factors associated with childhood asthma in children who are the resident of Karachi when they exposed to a particular environment and investigate the main risk factors.

MATERIALS AND METHODS

This clinical-based study was conducted at the Agha Khan University Hospital in Karachi from November 2020 to November 2021. The participants were the 500 children of age 2 months to 12 years who attended the pediatrics Department of Agha Khan University Hospital in Karachi. Children were divided into two group based on observations and clinical record, one group of asthmatic patients consist of 250 participants while the second group which was a control group also contained 250 non-asthmatic patients and all 500 children were residents of Karachi and nearby areas, Pakistan.

Inclusion criteria:

Children with good compliance between the ages of 2 months to 12 years who met the diagnostic criteria for bronchial asthma in children were part of the study.

Exclusion criteria:

Persons with primary or secondary immunodeficiency, combine with other serious diseases such as liver and kidney failure, and arrhythmia. Persons had throat disease, pulmonary tuberculosis, bronchial pneumonia, congenital heart disease, and abnormal respiratory system structure were not included in this study.

Data collection:

A self-administered questionnaire was used to collect the data from the parents of children. The questionnaire divided into two sections, first section based on questions about the name, age, and gender, second section related to disease such as the family history of asthma/allergy, and other risk factors namely as environmental factors(new house renovation, passive smoking, weather changes, pet feeding history), Self-factors (obesity, repeated respiratory infections, history of allergies, early use of antibiotics in infants and young children, premature delivery, low birth weight) and pregnancy factors(breastfeeding, cesarean section)and other aspects. Questionnaire was developed in English and Urdu language (for those who are from urban areas and unable to read and understand English) and tested on all participants. At the end of the questionnaire a contest was signed by each parent of participant and physicians.

Statistical analysis:

In this study, SPSS version 22.0 statistical software was used to analyze and process the data. Count data were expressed as n/%, with X²-test, measurement data were expressed as $x \pm s$, and t-test was performed. Logistic multiple regression analysis was used to analyze the risk factors of childhood asthma and statistically significant results were express as $P < 0.05$.

RESULTS

Table.1 elucidate all the factors in the two groups. Of the 500 cases, 250 (50%) were asthmatic cases and 250 (50%) were non-asthmatic. Among the asthmatic cases, 146 (58.4%) were females and 104 (41.6%) were males, 138(55.2%) had a family history of allergies and 149(59.6) had a family history of asthma,

asthmatic patients were influenced by other factors including environmental factors (Passive smoking 155(62%), weather changes 143(57.2%), 93(37.2), new house renovation 111(44.4%)), self-factors (obesity 89(35.6%), exposure to antibiotics 104(41.6%), repeated respiratory infections 151(60.4%), pregnancy factors (Cesarean section 43(17.2%), Premature delivery 46 (18.4%). Low birth weight 73(29.2%) and while breastfeeding had no association with asthma ($p= 0.081$), 112 (44.8%) asthmatic patients who had no history of allergies and 101 (40.4%) had no history of asthma were significantly associated with childhood asthma ($P<0.05$).

Multiple regression analysis (Table.2) was performed on all given factors and concluded that patients had history of allergies (OR= 3.51, 95% CI= 2.67-4.78), and asthma (OR= 4.6, 95% CI= 2.51-5.62, $P<0.05$) were strongly associated with development of asthma in childhood. From the environmental factors passive smoking had great contribution to develop childhood asthma (OR= 3.14, 95%CI= (2.21-4.42)), new house renovation (OR= 1.45, 95%CI=1.31-1.69), weather changes (OR= 0.21, 95% CI= 0.61-0.89), and pet feeding history (OR= 1.14, 95% CI= 0.73-1.75), also had significant association with childhood asthma. Modestly association was found with obesity (OR=0.09, 95%CI= 0.21-1.02), and cesarean section (OR= 0.25, 95% CI= 0.10-1.49). Breast feeding (OR= 0.64, 95% CI= 0.35-0.39) had no association with asthma while premature delivery (OR=2.90, 95%CI=1.09-3.02) low birth weight (OR=2.61, 95%CI=2.31-2.62) and early exposure to antibiotic in infant and young children (OR=1.46, 95%CI= 1.46-2.99) had significant association.

Table.3 all the factors had an indispensable role in enhanced asthma in children. Family history had a mean value 149.5 ± 0.59 with p -value <0.001 that mean patients with a family history of asthma were greater, similarly environmental factor was found more common in asthma patients 135.5 ± 0.78 . Self-factor (123.6 ± 0.77) and pregnancy factor (93 ± 0.65) also had significant $p<0.05$ impact

DISCUSSION

In our study family history, environmental exposure, and pregnancy-related factors had a prominent impact to increase the risk of childhood asthma. A study had a similar finding to our study as 47% of children exhibited asthma and allergy family history and 41.5% had a history of passive smoking.⁶ Cigarette smoke was deemed most worse risk factor among all the environmental factors which badly induced the respiratory disorder like asthma in children.⁷ Exposure to tobacco was causation that frequently involves the reduction of lung function and induces exacerbation. Therefore, current asthma treatment guidelines suggest shunning tobacco smoke.²³ Individual had a genetic history of asthma then environmental factor strongly influence.⁸ in our study 40.4% asthmatic children did not found with a history of asthma that might be asthmatic because of genetic factors. Pets at home were associated with asthma in children. Evidence identified had a positive relation with pets in the development of asthma in children such as exposure of children to cats at age of 6 years could be a risk to develop asthma.¹² Different weather had a varying effect on asthma, spring and winter reported with the greater effect such as OR= 1.53 and OR= 1.10.²⁴

House renovation was another variable that substantially affects the asthma prevalence. A study demonstrated that household renovation had an association with premature birth and low birth weight, and children were found to be more vulnerable to childhood asthma.¹ Child was more susceptible to renovated items as a high odd ratio was noticed in the literature to develop asthma.² A cohort study concluded that renovation material could be a reason to increase the risk of childhood asthma.³ However, more researches are needed to verify the child's exposure to renovation pollutants either during or after the pregnancy that imposed the adverse effect on children health-related to asthma. The present study found no contribution of breastfeeding in the development of childhood asthma. Breastfeeding did not have a clear relationship with asthma, many studies show the beneficial effects of breastfeeding such as most protective against the lower respiratory tract.⁴ Immunoglobulins of human breast milk have a protective role.⁵ Postnatal exposure to antibiotics could enhance the risk of childhood asthma in early life.⁹ A cohort study reported wheezing at age 4 years could be a reason of asthma at 6 years if children experience rhinovirus.¹⁰ One more study associated with risk of asthma in cases children found rhinovirus positive, wheezing during the infancy that could prone the children to asthma at age 5 years.¹¹ The patients having a history of asthma were commonly experienced wheezing and exacerbation in young children when they suffered from viral respiratory infection.²⁵⁻²⁶

One more pediatric literature identifies the greater association of cesarean delivery (OR= 2.6) with asthma in children as compared to vaginal birth (OR=1.3) but its underlying mechanism needs to be more elucidated. It also identified the positive relationship with low birth weight.¹³ Premature delivery and low birth weight both factors to some extent are closely associated with each other and with the risk of pediatric asthma. A study demonstrated that asthmatic mothers were not associated with premature birth but premature birth was associated with the development of asthma in children early and later life. Premature delivery enhanced the risk of respiratory morbidity in childhood.¹⁴ An independent relation was found between birth weight and pediatric asthma with a high risk of prevalence in African American children.¹⁵ The prevalence of obesity and asthma had been significantly high in many countries, epidemiological studied in children concluded a positive relation of body mass index and asthma, on the other hand, no evidence was found that asthma leads to increase obesity.¹⁹

CONCLUSION

This study elucidated that childhood asthma is a multifactorial heterogeneous disorder, where family history, environmental factors, self-factors, and pregnancy factors all had a substantial role to enhance the number of cases of asthma, especially in children. Among the pregnancy factor, breastfeeding had a non-significant impact on the development of asthma in childhood. We can overcome this issue through the proper treatment and management with the cooperation of physicians who are handling such cases and can improve the quality of life.

Factors		Asthmatic children (n=250) N(%)	Control group (n=250) N(%)	X ² test	p-value
Age (≥ 2 months-≤ 12 years)	-----	250(100)	250(100)	-----	-----
Gender	Males	104 (41.6)	132 (52.8)	5.31	0.031
	Females	146 (58.4)	118 (47.2)		
Family factors					
History of allergies	Yes	138 (55.2)	29 (11.6)	4.78	0.029
	No	112 (44.8)	221 (88.4)		
History of asthma	Yes	149 (59.6)	28 (11.2)	5.22	0.034
	No	101 (40.4)	222 (88.8)		
Environmental factors					
New house renovation	Yes	111 (44.4)	156 (62.4)	6.21	0.043
	No	139 (55.46)	94 (37.6)		
Passive smoking	Yes	155 (62)	89 (35.6)	3.14	0.010
	No	95 (38)	161 (64.4)		
Weather changes	Yes	143 (57.2)	76 (30.4)	4.38	0.032
	No	107 (42.8)	174 (69.6)		
Pet feeding history	Yes	93 (37.2)	56 (22.4)	5.32	0.021
	No	157 (62.8)	194 (77.6)		
Self-factors					
Obesity	Yes	89 (35.6)	73 (29.2)	5.97	0.039
	No	161 (64.4)	177 (70.8)		
Repeated respiratory infections	Yes	151(60.4)	18 (7.2)	1.99	0.001
	No	99(39.6)	232 (92.8)		
Early exposure to antibiotics in infants and young children	Yes	104 (41.6)	34 (13.6)	3.09	0.029
	No	146 (58.4)	216 (86.4)		
Pregnancy factors					
Cesarean section	Yes	43 (17.2)	41 (16.4)	3.11	0.032
	No	207 (82.8)	209 (83.6)		
Premature delivery	Yes	46 (18.4)	6 (2.4)	5.56	0.042
	No	204 (81.6)	244 (97.6)		

Low birth weight	Yes	73 (29.2)	19 (7.6)	7.48	0.021
	No	177 (70.8)	231 (92.4)		
Breast feeding	Yes	210 (84)	240 (96)	12.79	0.081
	No	40 (16)	10 (4)		

N= number of cases.

Table 1: General risk factor for both asthmatic and non-asthmatic group

Variables	Regression Coefficient	Mean Standard Error (S.E)	OR (95% CI)	p-value
Age	0.427	0.189	1.47 (0.95-1.99)	0.036
Gender	-0.702	0.193	1.43 (0.35-0.58)	0.001
Family factors				
History of allergies	1.49	0.056	3.51(2.67-4.78)	<0.05
History of asthma	1.46	0.054	4.6(2.51-5.62)	<0.05
Environmental factors				
New house renovation	0.122	0.194	1.45(1.31-1.69)	<0.05
Passive smoking	1.082	0.187	3.14(2.12-4.42)	<0.05
Weather changes	0.321	0.212	0.21(0.61-1.89)	<0.05
Pet feeding history	-0.469	0.205	1.14(0.73-1.75)	<0.05
Self-factors				
Obesity	0.420	0.781	0.09(0.21-1.02)	<0.05
Repeated respiratory infections	1.563	0.346	2.56(1.04-3.35)	<0.05
Early exposure to antibiotics in infants and young children	1.682	0.431	1.46(1.14-2.99)	<0.05
Pregnancy factors				
Cesarean section	1.193	0.245	0.25(0.10-1.49)	<0.05
Premature delivery	1.213	0.921	2.61(1.09-3.02)	<0.05
Low birth weight	1.129	0.021	2.90(2.31-2.62)	<0.05
Breast feeding	-0.986	0.687	0.64(0.35-0.39)	0.09

Table 2: Multiple logistic regression analysis

Variables	X ± S.E	P-value
Age	10.5 ± 0.33	<0.05
Family factor	149.5 ± 0.59	<0.001
Environmental factor	135.5 ± 0.78	<0.001
Self-factor	123.6 ± 0.77	<0.05
Pregnancy factor	93 ± 0.65	<0.05

T-test was applied to obtain the mean values. X= mean, S.E= Standard Error

Table 3: overall contribution of different risk factors in development of asthma in asthmatic group

REFERENCES

1. Leung, J.Y., Lam, H.S., Leung, G.M., Schooling, C.M., 2016. Gestational age, birthweight for gestational age, and childhood hospitalizations for asthma and other wheezing disorders. *Paediatr. Perinat. Epidemiol.* 30, 149–159. (<https://pubmed.ncbi.nlm.nih.gov/26739588/>)
2. Herberth, G., Gubelt, R., Röder, S., Krämer, U., Schins, R.P., Diez, U., Borte, M., Heinrich, J., Wichmann, H.E., Herbarth, O., Lehmann, I., LISA plus study group, 2009. Increase of inflammatory markers after indoor renovation activities: the LISA birth cohort study. *Pediatr. Allerg. Immunol.* 20, 563–570. (<https://europepmc.org/article/MED/18312535>)
3. Zhang, J., Sun, C., Liu, W., Zou, Z., Zhang, Y., Li, B., ... & Huang, C. (2018). Associations of household renovation materials and periods with childhood asthma, in China: A retrospective cohort study. *Environment international*, 113, 240-248. (<https://pubmed.ncbi.nlm.nih.gov/29454245/>)
4. Wright AL, Holberg CJ, Taussig LM, Martinez FD. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax* 2001; **56**:192–7. (<https://pubmed.ncbi.nlm.nih.gov/11182011/>)
5. Palmer LJ, Celedón JC, Weiss ST, Wang B, Fang Z, Xu X. *Ascaris lumbricoides* infection is associated with increased risk of childhood asthma and atopy in rural China. *Am J Respir Crit Care Med* 2002; **165**:1489-93. (<https://pubmed.ncbi.nlm.nih.gov/12045121/>)
6. Mubashar Y, Hussain W, Maqbool S. Distribution of risk factors in children with bronchial hyper reactivity. *Pak Paed J* 2000;24:61-4. (<https://jpma.org.pk/article-details/7381>)
7. Pirastu R, Bellu C, Greco P, Pelosi U, Pistelli R, Accetta G, et al. Indoor exposure to environmental tobacco smoke and dampness: respiratory symptoms in Sardinian children–DRIAS study. *Environ Res.* 2009; 109: 59-65
8. Karunasekera, K. A. W., Jayasinghe, J. A. C. T., & Alwis, L. W. G. R. (2001). Risk factors of childhood asthma: a Sri Lankan study. *Journal of Tropical Pediatrics*, 47(3), 142-145. (<https://academic.oup.com/tropej/article/47/3/142/1728771>)
9. Murk W, Risnes KR, Bracken MB. Prenatal or early-life exposure to antibiotics and risk of childhood asthma: a systematic review. *Pediatrics* 2010;127:1125–38. (<https://pubmed.ncbi.nlm.nih.gov/21606151/>)

10. Jackson DJ, Gangnon RE, Evans MD, et al. Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. *Am J Respir Crit Care Med* 2008;178:667–2. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2556448/>)
11. Kusel MM, de Klerk NH, Keadze T, et al. Early-life respiratory viral infections, atopic sensitization, and risk of subsequent development of persistent asthma. *J Allergy Clin Immunol* 2007;119:1105–10. (<https://pubmed.ncbi.nlm.nih.gov/17353039/>)
12. Torrent M, Sunyer J, Garcia R, Harris J, Iturriaga MV, Puig C, Vall O, Anto JM, Newman Taylor AJ, Cullinan P. Early-life allergen exposure and atopy, asthma, and wheeze up to 6 years of age. *American journal of respiratory and critical care medicine*. 2007 Sep 1;176(5):446-53. (<https://www.atsjournals.org/doi/full/10.1164/rccm.200607-916OC>)
13. Lavin T, Franklin P, Preen DB. Association between caesarean delivery and childhood asthma in India and Vietnam. *Paediatric and perinatal epidemiology*. 2017 Jan;31(1):47-54. (<https://pubmed.ncbi.nlm.nih.gov/28029700/>)
14. Kelly YJ, Brabin BJ, Milligan P, Heaf DP, Reid J, Pearson MG. Maternal asthma, premature birth, and the risk of respiratory morbidity in schoolchildren in Merseyside. *Thorax*. 1995 May 1;50(5):525-30. (<https://pubmed.ncbi.nlm.nih.gov/7597666/>)
15. Brooks AM, Byrd RS, Weitzman M, Auinger P, McBride JT. Impact of low birth weight on early childhood asthma in the United States. *Archives of pediatrics & adolescent medicine*. 2001 Mar 1;155(3):401-6. (<https://pubmed.ncbi.nlm.nih.gov/11231809/>)
16. Bosonea AM, Sharpe H, Wang T, Bakal JA, Befus AD, Svenson LW, Vliagoftis H. Developments in asthma incidence and prevalence in Alberta between 1995 and 2015. *Allergy, Asthma & Clinical Immunology*. 2020 Dec;16(1):1-1. (<https://pubmed.ncbi.nlm.nih.gov/33061999/>)
17. Hernández-Garduño E. Asthma mortality among Mexican children: Rural and urban comparison and trends, 1999-2016. *Pediatric pulmonology*. 2020 Apr;55(4):874-81. (<https://onlinelibrary.wiley.com/doi/abs/10.1002/ppul.24658>)
18. Ding G, Ji R, Bao Y. Risk and protective factors for the development of childhood asthma. *Paediatric respiratory reviews*. 2015 Mar 1;16(2):133-9. (<https://pubmed.ncbi.nlm.nih.gov/25155282/>)
19. Gern JE. The urban environment and childhood asthma study. *Journal of Allergy and Clinical Immunology*. 2010 Mar 1;125(3):545-9. (<https://pubmed.ncbi.nlm.nih.gov/20226291/>)
20. Chinn S. Obesity and asthma: evidence for and against a causal relation. *Journal of Asthma*. 2003 Jan 1;40(1):1-6. (<https://pubmed.ncbi.nlm.nih.gov/12699207/>)
21. Zhao, Z.H., Zhang, X., Liu, R.R., Norback, D., Wieslander, G., Chen, J., Sundell, J., 2013. Prenatal and early life home environment exposure in relation to preschool children's asthma, allergic rhinitis and eczema in Taiyuan, China. *Chin. Sci. Bull.* 58, 4245–4251 (<https://www.researchgate.net/publication/257689534>)
22. Lin, Z.J., Norback, D., Wang, T., Zhang, X., Shi, J., Kan, H., Zhao, Z., 2016. The first 2- year home environment in relation to the new onset and remission of asthmatic and allergic symptoms in 4246 preschool children.

- Sci. Total Environ. 553, 204–210.
(<https://www.sciencedirect.com/science/article/abs/pii/S0048969716302510?via%3Dihub>)
23. Yoo S, Kim HB, Lee SY, Kim BS, Kim JH, Yu J, Kim BJ, Lee DH, Seong MW, Hong SJ. Effect of active smoking on asthma symptoms, pulmonary function, and BHR in adolescents. *Pediatr Pulmonol* 2009;44(10):954–61. (<https://pubmed.ncbi.nlm.nih.gov/19728392/>)
24. Han YY, Lee YL, Guo YL. Indoor environmental risk factors and seasonal variation of childhood asthma. *Pediatric Allergy and Immunology*. 2009 Dec;20(8):748-56. (<https://pubmed.ncbi.nlm.nih.gov/19236600/>)
25. MacDowell AL, Bacharier LB. Infectious triggers of asthma. *Immunol Allergy Clin North Am* 2005;25(1):45–66. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7118995/>)
26. Carroll KN, Hartert TV. The impact of respiratory viral infection on wheezing illnesses and asthma exacerbations. *Immunol Allergy Clin North Am* 2008;28(3):539–61. (<https://pubmed.ncbi.nlm.nih.gov/18572106/>)