ROLE OF VIRAL INFECTIONS IN THE DEVELOPMENT AND EXACERBATION OF ASTHMA IN CHILDREN

Dr Sadia Munir, Dr Uzair Asad, Dr Osama Zahid Khokhar.

1MBBS, Liaquat National Medical College and Hospital, Karachi., 2,3MBBS, Nawaz Sharif Medical College, Gujrat.

Abstract:
Viral infections are very common in young children. In early ages, viral infections due to respiratory syncytial virus (RSV) and human rhinovirus (HRV), have a significant relation with asthma. Bronchiolitis and irregular wheezing lead to the development and exacerbation of asthma. Severe asthmatic conditions require acute care because it is a major cause of morbidity in children of 1 to 6 years. In this study, the role of viral infections in asthma development in children is noticed by collecting the information about the risk factors and statistical informations as well. The therapeutic strategies for the prevention and treatment of viral infections and asthma is also discussed below.

Corresponding author:
Dr. Sadia Munir,
MBBS, Liaquat National Medical College and Hospital, Karachi.

Please cite this article in press Sadia Munir et al. Role Of Viral Infections In The Development And Exacerbation Of Asthma In Children., Indo Am. J. P. Sci, 2020; 07(12).
INTRODUCTION:
Bronchiolitis, intense wheezing ailments, and asthma are a colossal clinical weight. In the first year of life, the pervasiveness of bronchiolitis is around 20% to 30% and in the second year of life, it is 10% to 20%[1, 2]. Up to 30% to half of the children have acute wheezing in any event once before school age, of these, 30% to 40% will have irregular wheezing[1]. In the end, the pervasiveness of asthma in growing children is approximately 5% to 10%[3]. In early life, approximately all children are tainted with a respiratory infection, and the greater of them experience related lower respiratory tract (LRT) illness, which is clinically shown as wheezing or different indications of respiratory trouble, before school age[4]. Using sub-atomic diagnostics, a viral microbe can be distinguished in most of the wheezing scenes that happen in the initial 5 years of life[5]. The most well-known infections related to these beginning stages wheezing scenes are respiratory syncytial infection (RSV), human rhinovirus (HRV), and human metapneumovirus para influenza, and coronavirus[6]. Viral respiratory lot contaminations can have significant effects on significant parts of asthma. For most newborn children, wheezing scenes with respiratory diseases decrease with age, yet for certain people, wheezing scenes in early life can stamp the start of asthma[7].

Respiratory viral contaminations can have serious antagonistic results in patients with setting up asthma; viral respiratory diseases are related to almost 80% of asthma intensification episodes[8]. The relationship between viral respiratory contaminations and asthma intensifications is observed in both kids and grown-ups[7]. In research, solid proof for an important role of respiratory infections in the development of asthma in youngsters is given. Exemplary investigations demonstrated that respiratory syncytial infection (RSV) bronchiolitis, sufficiently serious to require hospitalization, is a danger factor for asthma at the age of 7, 13, and 18[9]. In comparison with HRV negative cases asthma at 6 years being more than four-overlap higher[10].

Recent research shows that the diagnostics of viral respiratory parcel diseases have improved given the advancement of PCR methods. A few new respiratory infections and their subgroups have been found, and particularly rhinovirus (RV) diagnostics have uniquely improved[11]. It has been discovered that bronchiolitis and early wheezing scenes are quite often (90% to 100% of cases) related to viral diseases[12]. The purpose of this review is to focus on the key factors by the viral infections that play important role in the development and exacerbation of asthma in children. Similarly to have a look at the strategies for prevention and treatment of asthma.

Development and Exacerbations of Asthma:
Asthma is known as a chronic disorder in which mucus secretion is increased. It is characterized by airway inflammation and bronchial hyperresponsiveness, all of which cause reversible airflow obstruction[13]. The epithelium problems and constant irritations in asthma are due to numerous ecological factors. For example, viral contaminations, allergens environmental impacts, and genetic impacts.

Role of Viral Infections:
Research shows that the most widely recognized reason for episodic wheezing in young children is respiratory viral infections. Especially during the winter season initial studies focused on the role of respiratory syncytial virus (RSV) and as the predominant microbe related to bronchiolitis. Longitudinal investigations showed that RSV bronchiolitis builds the danger of repetitive wheezing and asthma in little youngsters[14, 15]. Even though the Tucson Children's Respiratory Study has demonstrated that this danger diminishes logically with age and is no longer significant by age 13[15], different examinations show that RSV bronchiolitis sufficiently serious to cause hospitalization for hypersensitive asthma into pre-adulthood.

There is presently clear proof that other viral sorts are additionally connected with bronchiolitis and wheezing. Although human metapneumovirus, influenza, and parainfluenza are connected with scenes of wheezing [4], a few late examinations demonstrate that the predominant microbe other than RSV identified during such scenes, especially in kids more seasoned than 6 mo old enough, is human rhinovirus (HRV) [16]. Apparently, HRV contaminations offer more generously to asthma improvement than was recently valued. Not just has it been accounted for those youngsters hospitalized with HRV-incited bronchiolitis are at especially high danger for resulting development of asthma[17], however, in a new report, HRV-instigated lower respiratory disease during early stages was the absolute most significant hazard factor for ensuing advancement of youth wheezing.

Recent studies demonstrate that the intense exacerbations of asthma represent half of the all-out medical services costs related to this sickness and lead to the passings of some 5,000 Americans every year[18]. Research provides a piece of evidence that
Exacerbations of asthma are associated with upper respiratory tract viral infections (URI) which is a predominant risk factor[19]. There is a clear time-related connection between flare-ups of URI and expansions in hospitalizations for asthma exacerbations[19, 20].

**Viral Infections in Early Ages and Asthma:**
Research shows that in the initial 2 years of life practically all children are seropositive for RSV, while the clinical appearances of contamination are a major factor. A major clinical test that outcomes after RSV disease in babies and preschool youngsters identify with its long haul sequelae, which incorporate intermittent wheezing and the development of asthma. Studies show that there is a connection between RSV bronchiolitis to the development of wheeze and asthma in youth[21]. It has been demonstrated in studies that LRT infection with RSV resulting in bronchiolitis increases the 7.2-fold risk of asthma up to 18 years[22]. Statistical data regarding asthma development due to RSV-positive bronchiolitis highlighted the importance of the severity of the initial episode in contributing to the development of future asthma[21]. In early life studies, the RSV Bronchiolitis has planned accomplice of babies hospitalized for RSV bronchiolitis and spotlights on distinguishing indicators of post-RSV asthma. A great risk of Asthma is also connected to allergic sensitization at age 3 years[23]. The connection between baby age at their first winter viral peak following birth and resulting asthma hazard during the fifth and 6th year of life has been explored to address this inquiry. Babies who were 4 months old at the pinnacle of winter viral season were bound to create both bronchiolitis and youth asthma.

**Figure 1 Role of infections in asthma[7]**

**Figure 2 Childhood Origins of Asthma (COAST) study design[7]**
HRV wheezing diseases during the primary year of life were related with expanded asthma hazard at 5 years old years, although this finding was confined to kids who created aeroallergen sharpening by the age of 2 years[24]. In this way, two isolated and inconsequential birth companions have distinguished HRV wheezing sicknesses during the earliest stages and early aeroallergen refinement as danger factors for youth asthma improvement.

The age at which HRV wheezing ailments happen has a critical prognostic incentive concerning the resulting danger of asthma. Youngsters who wheezed with HRV during the principal year of life had a roughly three-crease danger of having asthma at 6 years old years. HRV wheezing in the subsequent year was related to a higher asthma hazard, and wheezing with HRV contamination during the third year of life was related to a high danger of creating asthma at young, with a chances proportion of 32[5].

RSV and rhinoviruses are identified as the risk factors in determining progression to asthma. The comparison of these viral infection impacts on the children is shown in Table 1.

**Table 1. Comparison of Rhinovirus and Respiratory Syncytial Virus in asthma development[21]**

| Age | From first to third year of life risk increases. | Risk increase in first year of life, especially under 6 months |
| --- | --- | --- |
| Illness severity | No obvious impact on risk of asthma | More severe disease increased the risk of asthma |
| Parental atopy | Increased risk of asthma | Increased asthma risk with maternal atopy |
| Early allergic sensitization and prevalence of atopy (eczema or hayfever) | Predisposition to rhinovirus infection and subsequent asthma | Associated with increased risk of asthma development |
| Immune responses to re-infection | Unknown | Early infection in infancy skews immune responses towards Th2 phenotype with subsequent infection later in life |
| Lung-function deficit | Early deficit present at birth, or following infections in the first 3 years of life, may increase risk of asthma | Early deficit present at birth, or resulting from first severe infection, leads to increased risk of asthma |
Therapeutic Measures for the Treatment of Viral Infections and Asthma:
There are different therapeutic measures for the prevention and treatment of viral infections and asthma. In childhood wheezing that is connected with viral infections, the present drug therapies are considered as less than ideal. The drugs for mild to moderate bronchiolitis are best at this stage but do not affect the duration of hospitalization[25]. The drugs used for this are Bronchodilators. On the other hand, the montelukast drug is used to reduce the number of virally induced asthma exacerbations in young children with irregular asthma[18].

In adults, the utilization of corticosteroids, alone and in blend with long-acting - agonists, or leukotriene receptor foes to keep up ideal asthma control, has demonstrated efficacious in diminishing quantities of asthma intensifications, and the utilization of oral corticosteroids right off the bat in intensifications forestalls backslides. An undeniable elective technique is to utilize antiviral methodologies[18]. Influenza vaccine is compelling in forestalling illness intensifications initiated by this infection throughout the cold weather months, yet immunization approaches have not been effective for RSV and are not attainable for HRV, give the huge number of viral serotypes[18].

Respiratory infections connect with having ecological components to expand the danger of wheezing ailments in babies and to build the danger of intensifications in asthmatic youngsters[13]. These discoveries recommend that there are various remedial occasions to decrease the recurrence and seriousness of viral respiratory ailments and ideally optional impacts on the occurrence and intensification of asthma[13] (Fig.4).

As we keep on picking up more noteworthy experiences into the instruments by which viral contaminations upgrade creation of specific proinflammatory cytokines, and into endogenous systems of host defense, alternative therapeutics strategies might be derived[18]. These could go from specific inhibitors of key virally actuated flagging pathways in epithelial cells to enemies of specific chemokines that may assume a critical part in pathogenesis. At long last, improvement of endogenous host antiviral pathways, or skin organization of medications, for example, nitric oxide givers, may give elective ways to deal with diminish virally prompted inflammation.

CONCLUSION:
There is solid, reproducible information that respiratory infections, particularly HRV, are related to and most likely significant in the turn of events and intensification of asthma. The results of statistical data represent that children at an early age are at greater risk of developing asthma with HRV infections. On the other hand use of different treatments, e.g antiviral for RSV and HRV can decrease the risk factors for asthma.

REFERENCES:
1. Taussig, L.M., et al., Tucson children's respiratory study: 1980 to present. Journal of
Allergy and Clinical Immunology, 2003. 111(4): p. 661-675.
2. Awad, S., et al., Viral surveillance of children with acute respiratory infection in two main hospitals in Northern Jordan, Irbid, during winter of 2016. Journal of pediatric infectious diseases, 2020. 15(1): p. 1.
3. Lai, C.K., et al., Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax, 2009. 64(6): p. 476-483.
4. Jartti, T., et al., Respiratory picornaviruses and respiratory syncytial virus as causative agents of acute expiratory wheezing in children. Emerging infectious diseases, 2004. 10(6): p. 1095.
5. Jackson, D.J., et al., Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. American journal of respiratory and critical care medicine, 2008. 178(7): p. 667-672.
6. Calvo, C., et al., Role of rhinovirus in hospitalized infants with respiratory tract infections in Spain. The Pediatric infectious disease journal, 2007. 26(10): p. 904-908.
7. Busse, W.W., R.F. Lemanske Jr, and J.E. Gern, Role of viral respiratory infections in asthma and asthma exacerbations. The Lancet, 2010. 376(9743): p. 826-834.
8. Johnston, S.L., et al., Community study of the role of viral infections in exacerbations of asthma in 9-11-year-old children. BMJ, 1995. 310(6989): p. 1225-1229.
9. García-García, M., et al., Human metapneumovirus bronchiolitis in infancy is an important risk factor for asthma at age 5. Pediatric pulmonology, 2007. 42(5): p. 458-464.
10. Kotaniemi-Syrjänen, A., et al., Rhinovirus-induced wheezing in infancy—the first sign of childhood asthma? Journal of Allergy and Clinical Immunology, 2003. 111(1): p. 66-71.
11. Jartti, T., et al., New molecular virus detection methods and their clinical value in lower respiratory tract infections in children. Pediatric respiratory reviews, 2013. 14(1): p. 38-45.
12. Turunen, R., et al., The first wheezing episode: respiratory virus etiology, atopic characteristics, and illness severity. Pediatric Allergy and Immunology, 2014. 25(8): p. 796-803.
13. Jartti, T. and J.E. Gern, Role of viral infections in the development and exacerbation of asthma in children. Journal of Allergy and Clinical Immunology, 2017. 140(4): p. 895-906.
14. Sigurs, N., et al., Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7. American journal of respiratory and critical care medicine, 2000. 161(5): p. 1501-1507.
15. Stein, R.T., et al., Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. The Lancet, 1999. 354(9178): p. 541-545.
16. Heymann, P.W., et al., Viral infections to age, atopy, and season of admission among children hospitalized for wheezing. Journal of allergy and clinical immunology, 2004. 114(2): p. 239-247.
17. Reijonen, T.M., et al., Predictors of asthma three years after hospital admission for wheezing in infancy. Pediatrics, 2000. 106(6): p. 1406-1412.
18. Proud, D. and C.-W. Chow, Role of viral infections in asthma and chronic obstructive pulmonary disease. American journal of respiratory cell and molecular biology, 2006. 35(5): p. 513-518.
19. Johnston, S.L., et al., The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. American journal of respiratory and critical care medicine, 1996. 154(3): p. 654-660.
20. Johnston, N.W., et al., The September epidemic of asthma hospitalization: school children as disease vectors. Journal of Allergy and Clinical Immunology, 2006. 117(3): p. 557-562.
21. Saglani, S., Viral infections and the development of asthma in children. Therapeutic advances in infectious disease, 2013. 1(4): p. 139-150.
22. Sigurs, N., et al., Asthma and allergy patterns over 18 years after severe RSV bronchiolitis in the first year of life. Thorax, 2010. 65(12): p. 1045-1052.
23. Bacharier, L.B., et al., Determinants of asthma after severe respiratory syncytial virus bronchiolitis. Journal of Allergy and Clinical Immunology, 2012. 130(1): p. 91-100. e3.
24. Kusel, M.M., et al., Early-life respiratory viral infections, atopic sensitization, and risk of subsequent development of persistent asthma. Journal of Allergy and Clinical Immunology, 2007. 119(5): p. 1105-1110.
25. Patel, H., S. Gouin, and R.W. Platt, Randomized, double-blind, placebo-controlled trial of oral albuterol in infants with mild-to-moderate acute viral bronchiolitis. The Journal of pediatrics, 2003. 142(5): p. 509-514.