The Role of Respiratory Syncytial Virus in Asthma Flare-Ups in Children: A Hospital-Based Study

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ABSTRACT:

BACKGROUND:

Bronchial asthma is a chronic inflammatory disease of the respiratory tract constituting a serious public health problem all over the world. The most common trigger in childhood asthma is viral URTIs. Studies have shown that viruses are associated with 80 to 85% of asthma exacerbations in school-age children in the community including, rhinovirus, enterovirus, human metapneumovirus, echovirus, RSV and others. [1,2]

OBJECTIVE:

To study the prevalence of RSV infection in the acute asthmatic flare-ups in children 2-15 years of age.

PATIENTS AND METHODS:

A prospective, age and sex-matched case-control study, examined 90 children aged 2-15 years; 50 of them were asthmatics and 40 were non-asthmatics visited the outpatient clinic in the period from July to Dec. 2013. Children who had 3 or more attacks of wheezing LRTI diagnosed by a pediatrician as cases of asthma and showed a definite response to bronchodilator therapy were included in the asthmatic group. Parents and patients were interviewed and a well-structured questionnaire that solicited to their demographical and clinical characteristics was used. Blood samples were taken from all cases and controls and sent for ELISA test for anti-RSV IgM, IgG and IgA antibodies.

RESULTS:

There was no significant association between each of the RSV immunoglobulins detected and asthma flare-up between asthmatics and controls. There were no significant associations between each of residence, maternal smoking and history of fever and RSV infection between asthmatics and controls.

CONCLUSION:

There is a minor role in RSV infection as a triggering factor in asthma flare-ups in children aged 2-15 years.

KEYWORDS: Respiratory syncytial virus, Asthma, Children

INTRODUCTION:

Asthma is the most common chronic disease of childhood, with up to 20% of children being affected. All phenotypes of asthma are multifactorial disorders, which are the result of a complex interplay between genetic and environmental factors [1]. Infections can trigger atopic asthma, and atopy can cause wheezing during airway infections and modify the course of airway infections [2].

Viral respiratory tract infections have been the major cause of asthma exacerbations in children with reported prevalence rates of 85% in exacerbations of childhood asthma [3]. For those with existing asthma, exacerbations are a major cause of morbidity, can need acute care, and can, albeit rarely, result in death. The association of viral infections with exacerbations of wheeze in children with asthma has been reported in temperate climates with higher rates. For patients at risk of asthma, or with existing asthma, viral respiratory tract infections can have a profound effect on the expression of disease or loss of control.

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Viral respiratory tract infections, predominantly those caused by human rhinoviruses, are associated with asthma exacerbations. In view of the effect of respiratory viruses on many aspects of asthma, efforts to understand the mechanisms and risk factors by which these airway infections cause changes in airway pathophysiology are a first step towards improved treatment [4].

PATIENTS AND METHODS:

In this prospective case-control study, 90 age and sex-matched children were examined (their ages ranged from 2 years to 15 years). Among the studied children, 50 were asthmatics visited the outpatient clinic and/or admitted to Children Welfare Teaching Hospital (CWTH) and 40 were non- asthmatics visited the outpatient clinics for complaints other than asthma who were enrolled as a control group. The study's period was from July to Dec. 2013. Parents and children were interviewed (via a well-structured questionnaire that solicited to their demographical characteristics including age, sex, and residency). Clinical examination of the children including temperature measurements and chest examination were performed. The children included were those aged 2-15 years who had 3 or more attacks of wheezing LRTI (diagnosed by a pediatrician as cases of asthma who showed a definite response to bronchodilator therapy). Children with cardiopulmonary disease other than asthma were excluded from the study. Blood samples were taken from all cases and controls and sent for ELISA test for anti-RSV IgM, IgG and IgA antibodies. Data were statistically analyzed using SPSS program version 20. Chi-square was used as a test of significance for the qualitative data; P value≤0.05 was considered statistically significant.

RESULTS:

Fifty children with asthma aged 2-15 years were enrolled. The mean age was 6.63 years ± 3.45 SD; 35(70%) of them were males and 15(30%) were females and the mean number of asthmatic flare-ups 7.76 ± 3.87 SD. The control group of non-asthmatic children consists of 40 children with a mean age of 6.4 years ± 3.4 SD; 24 (60 %) of them were males and 16(40%) were females.

No significant difference was detected between cases and controls regarding age and sex, as shown in Table -1. No significant association between each of RSV IgM and IgG immunoglobulins detected by ELISA and asthma flare-ups in children, as shown in Table-2.

Five out of 22 (22.7%) children were from (2-5 years) age group, 11 out of 21(52.4%) children were from (>5-10 years) age group and 4 out of 7 (57.1%) children were from (>10-15 years) age group (P-value=0.08). Ten out of 21(47.6%) children were from (2-5 years) age group, 6 out of 10 (47.6%) were from (>5-10 years) age group and 3 out of 9 (33.3%) were from (>5-10 years) age group (P-value=0.5) (Table-3). Fourteen patients out of 20 (70%) asthmatic children with acute RSV infection were living in the urban area and the other six (30%) in rural area concluding that residence has no association with acute RSV infection in asthmatic children. There were no significant associations between each of residence, maternal smoking and fever with acute RSV infection (IgM positive) in asthmatic patients as shown in the Table -4. Twelve out of 19 (63.2%) non-asthmatic children with acute RSV infection were living in the urban area and the other seven (36.8%) in rural area concluding that residence has no association with acute RSV infection in non-asthmatic children, as shown in Table-5.

Table -1: Distribution of age and gender between asthmatics and controls

		Asthmatics		Nonasthmatics		Total	P-value
		No.	%	No.	%		
Gender	Male	35	70	24	60	59	0.32
	Female	15	30	16	40	31	
Mean age (years)± 2SD		6.63 ± 3.45		6.4 ± 3.4			0.62

Table -2: The Association of RSV infection (IgM and IgG positive ELIZA test) with asthma flare-ups and non-asthmatics

ELISA for RSV		Asthmatics		Non-asthmatics		Total	P-value
		No.	%	No.	%		
IgM	Positive	20	40	19	47	39	0.52
	Negative	30	60	21	52	51	
IgG	Positive	36	72	21	52	57	0.07
	Negative	14	28	19	47	33	

Table-3: Association of age groups with RSV infection (IgM positive) in asthmatics

	Age group	Positive IgM		Negative IgM		Total	P-value
		No.	%	No.	%		
Asthmatics	2-5 years	5	22.7	17	77.3	22	0.08
	>5-10 years	11	52.4	10	47.6	21	
	>10-15 years	4	57	3	43	7	
Non- asthmatics	2-5 years	10	47.6	11	52.4	21	0.5
	>5-10 years	6	60	4	40	10	
	>10-15 years	6	40	9	60	15	

Table-4: The association of risk factors with acute RSV infection (IgM positive) in asthmatics

		Positive IgM		Negative IgM		Total	P-value
		No.	%	No.	%		
Residence	Urban	14	43.7	18	56.3	32	0.339
	Rural	6	33.3	12	66.6	18	
Maternal smoking	Positive	13	68.4	19	31.6	32	0.574
	Negative	7	39	11	61	18	
Fever	Positive	10	43.3	13	56.5	23	0.431
	Negative	10	37	17	63	27	

Table-5: The association of risk factors with RSV infection in non- asthmatics

		Positive IgM		Negative IgM		Total	P- value
		No.	%	No.	%		
Residence	Urban	12	48	13	52	25	0.59
	Rural	7	46.7	8	53.3	15	
Maternal smoking	Positive	11	42.3	15	57.7	26	0.28
	Negative	8	57.1	6	42.9	14	

DISCUSSION:

Out of 50 children aged 2-15 years, seen in the outpatient clinic at CWTH with asthma flare-ups, 20 (40%) children had ELISA IgM positive for RSV. This result was higher than that reported by Freymuth et al [4] who reported 21.2% RSV infection in children hospitalized with an acute asthmatic flare-up, and Mathew et al [5] in Trinidad, who reported 2.9% of children with RSV infection, were much lower than what is reported in this study. Another study by Johnston et al[6] in Southhampton reported 9% RSV infection rate in acutely asthmatic children taking in consideration the age of the asthmatic children enrolled in the study between (9-11years). Maffey et al [7] reported that 40% of the asthmatic children were RSV positive. However, he included a younger age group in his study. The low yield of ELISA IgM positive for RSV in older children can be explained by the fact that most acute RSV infections occur in the first two years of life. By 2 years of age, almost all children have already been infected with RSV, and over half have been infected twice, [8] In addition to the geographical epidemiology of the virus, a study in Malaysia -noted by Ng et al[9]- reported that 85.8% of children with acute RSV infection were below the age of 2 years. Out of 40 non-asthmatic controls aged 2-15 years seen in the outpatient clinic at CWTH, 19(47%) children had ELISA IgM positive for RSV. This result is higher than that reported by Fattouh et al[10] in Egypt which was 16.4% and this might be attributed to the age of children enrolled in the Egyptian study (< 5years) and that the diagnosis was established by (IFA) of the nasal aspirate. Regarding age as a risk factor for acute RSV infection in asthmatic children, the present study concluded that there is no significant association between age and acute RSV infection in children aged 2-15 years with asthma flare-up. This agrees with Asner S et al [11] who reported that the younger age, was the factor that was most significantly associated with RSV infection patient among asthmatics. Considering the age as a risk factor for acute RSV infection , this study concluded that there is no association between age and acute RSV infection in non-asthmatic controls and this result is different from what reported in Egypt by Fattouh et al[10] who concluded that the RSV cases had significantly lower age mean than the non-RSV cases. We can explain this difference in the result by the age range that is between 8 days and 4 years taken by that study. This study reported that there is no significant association between fever and acute RSV infection in children with acute exacerbation of asthma. This result is not supported by Asner et al [11] study who concluded that RSV positive patients with an acute asthmatic exacerbation are significantly presented with fever. Ng et al [12] study on 450 non-asthmatic children admitted to hospital in Malaysia reported that fever had a significant association (84.2%) with acute RSV infection which disagrees with the result of this study. This difference might be attributed to the large difference in the number of patients enrolled in both studies. Fourteen patients out of 20 (70%) asthmatic children with acute RSV infection were living in the urban area and the other six (30%) in rural area concluding that residence has no association with acute RSV infection in asthmatic children. In this study, 12 out of 19 (63.2%) non asthmatic children with acute RSV infection were living in urban area and the other 7 (36.8%) in rural area concluding that residence has no association with acute RSV infection in non-asthmatic children. Wu A et al in Peru [12] study enrolled non-asthmatic patients reported that RSV infection was common in rural high altitude communities in Peru. This disagreement can be attributed to the geographical factor represented by high altitude and humidity in which other viruses are endemic. Thirteen patients out of 20 asthmatic children with acute RSV infection had positive history of maternal smoking showing no significant association with acute RSV infection in asthmatic patients. Out of the 19 non-asthmatic children with acute RSV infection, 11 patients had a positive history of maternal smoking that showed no significant association between maternal smoking and acute RSV infection in non-asthmatic children. This result agrees with Weber et al [13] in Gambia who reported that there was no association between maternal smoking and acute RSV infection.

CONCLUSION:

The role for RSV infection as a triggering factor in the flare-ups of asthma in children aged 2-15 years is minor.

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