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Research Article

Pattern of Viral Infection in Acute Asthma Exacerbation and Association with The Severity of The Episode

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Introduction: *Viral respiratory tract infections are very common among pediatric age groups and usually self-limited illnesses. Viral respiratory infections are associated with nearly 80% of asthma exacerbation episodes. For patients with existing asthma, viral respiratory tract infections can have a profound effect and can have severe adverse outcomes.*

Objectives: *To identify the prevalence of certain viruses in asthmatic children's during acute asthma exacerbation and identify any correlation between certain virus and severity of the episode.*

Methods: *A retrospective cross-sectional study was carried out including all children aged between 2 to 12 years who were admitted in royal hospital between January 2015 to October 2017 with acute exacerbation of asthma and who had nasal swab. Nasal swab was collected, which can detect 18 viruses like Rhinovirus, Boca virus, RSV A/B, Adenovirus respiratory, Human metapneumovirus, Coronavirus OC43, Parainfluenza 1, Parainfluenza 4, Influenza, Coronavirus 229E, Coronavirus HKU1, Parainfluenza 2, Parainfluenza 3, Influenza A (H1N1), Influenza A, Coronavirus NL63, Influenza B and Para echovirus.*

Results: *Among the 108 enrolled patients, viral infections were detected in 82 patients (75.9%). Rhinovirus is the most frequently detected virus (41%), followed by adenoviruses (13%), RSV (11%), boca virus (7%) and human metapnumovirus (6%). According to severity of asthma, viruses were detected in 6.1% of mild cases, 61% of moderate and 32.9 % of severe cases. No association between asthma severity and presence of virus (P=0.062). No significant difference in severe asthma exacerbation with or without viral infection. (32.9% vs. 53.8%) (P= 0.055) Among the viral-positive patients, Adenovirus has significant association with asthma severity (P= 0.021%). In our study, age, respiratory rate, and Oxygen saturation were significantly different between viral positive and viral negative group. (P values accordingly: 0.0001, 0.036, and 0.01).*

Conclusion: *Respiratory viruses were identified in 75.9% of patients with acute asthma exacerbation. Rhinovirus is the most frequently detected virus (41%), but adenovirus has significant association with asthma severity (P= 0.021%).*

Keywords: Acute exacerbation, Bronchial asthma, virus, viral infection, sputum.

Introduction

Asthma exacerbations are an exaggerated lower airway response to an environmental exposure [1]. Asthma is the most prevalent chronic respiratory disease worldwide, affecting more than 300 million people of all ethnic groups throughout all ages [2]. It is the most common chronic disease in children, imposing an increasingly consistent burden on health system [3].

Viral respiratory tract infections are the most common cause of wheezing illnesses and asthma exacerbations in both children and adults. virus infection is the most common environmental exposure to cause a severe asthma exacerbation [4]. For patients with existing asthma, viral respiratory tract infections can have a profound effect and can have severe adverse outcomes.

Acute respiratory tract infections are responsible for high morbidity and mortality, accounting for around 20% of the estimated 9 million deaths of children worldwide in 2007, according to the World Health Organization. Viruses are responsible for most of these infections, causing generally mild and self-limited infections, though some may become very severe or complicate the clinical course of patients with underlying chronic lung diseases, including asthma [5].

Moreover, the association between viral infection and environmental exposure is described as a trigger for exacerbations and type 2 inflammations are associated with an increased risk of virus-induced exacerbations [6]. The aim of this study was to identify the prevalence of certain viruses in asthmatic children's during acute asthma

exacerbation. And to look for any correlation between certain viruses and severity of asthma exacerbation.

Methods

This study was carried out in Royal hospital a tertiary hospital located in Muscat the capital city of Sultanate of Oman. Public health care is provided free of charge by the Ministry of health.

Study population

From January 2015 through October 2017, asthmatic children who have respiratory viral screen were included in our study if they met the following inclusion criteria: 2–12-year olds, admitted to hospitals and it is a retrospective cross-sectional study they have respiratory viral screen done & resulted. We only included in the study patients who are labeled as asthmatic by pediatrician. Asthmatic patients with: Congenital heart disease, chronic lung disease, Cystic fibrosis, Trisomy 21, Immunodeficiency, Neuromuscular diseases, chronic renal disease were excluded from our study as their diseases might affect the severity of asthma exacerbation.

All patients classified into three group according to asthma severity presentation in emergency department by using Pediatric asthma score system: Mild (score 1-2), Moderate (score 3-5), Sever (score 6-10). (Table 1).

Table 1:

Characteristic	0	1	2
Respiratory Rate **obtain over 30 sec, multiply by 2*			
2-3 years	≤34	35-39	≥40
4-5 years	≤30	31-35	≥36
6-12 years	≤26	27-30	≥31
>12 years	≤23	24-27	≥28
Oxygen requirement **obtain with pt on RA for 2 minutes*	≥93% on RA	89-92% on RA	≤88% on RA
Auscultation	Clear Breath Sounds	Expiratory Wheezes	Inspiratory & Expiratory wheezes or Diminished breath sounds
Work of Breathing - Nasal flaring - suprasternal muscle use - intracostal muscle use - subcostal muscle use	≤1 accessory muscle	2 accessory muscles	≥3 accessory muscles
Dyspnea	Speaks full sentences, playful, and takes PO well	Speaks partial sentences, short cry or poor PO	Speaks short phrases, grunting, or unable to PO

Data and sample collection

Data were collected from Royal Hospital electronic records (Al Shaifa system). A nasopharyngeal aspirate was obtained from each patient upon admission to the emergency department or in the pediatric ward. The nasopharyngeal swab specimens were obtained from the nostril from a depth of 2 to 3 cm by using a sterile ray swab that was then inserted into a vial containing 2.5 ml of viral transport medium. For the nasopharyngeal aspirate, a disposable catheter connected to a mucus extractor was inserted into the nostril to a depth of 5 to 7 cm and drawn back while applying gentle suction with an electric suction device.

Viral detection

Each sample was analysed using a Respiratory Panel I Viral Screening and Identification IFA Reagent immunofluorescence kit, consisting of a panel of monoclonal antibodies specific to influenza virus A (FLUVA), influenza virus B (FLUVB), human respiratory syncytial virus (hRSV), human adenovirus (hADV), and human parainfluenza viruses (hPIV) 1, 2, and 3 following the manufacturer's instructions and others viruses, total 14 different viruses.

Variables included in the study

We included in our study the following variables: Name of the patient & patient hospital number, Age of patient in in years, Gender, Nationality, Date of admission and length of stay. As well we included type of beds (Normal bed , high dependency & intensive care unit bed) , requirement of O2 therapy and its duration in days as well the presence of absence of Fever. Laboratory variables like complete white count, neutrophils count, lymphocyte count and C reactive protein were included. Chest x ray and its finding if done was as well included with either antibiotic or antiviral was used or not for each patient.

Results

During January 2015 to October 2017 with acute exacerbation of asthma, 380 childerns who disganosed to have asthma by physiotion and started on asthma prophlaxies. From this population, 108 were eligible to participate in the study. Among the 108 enrolled patients, viral infections were detected in 82 patients (76%). (Table 2) This was detected by using Respiratory viral panel PCR which is able to detect around 18 viruses in our hospital. (Table 2).

Table 2:

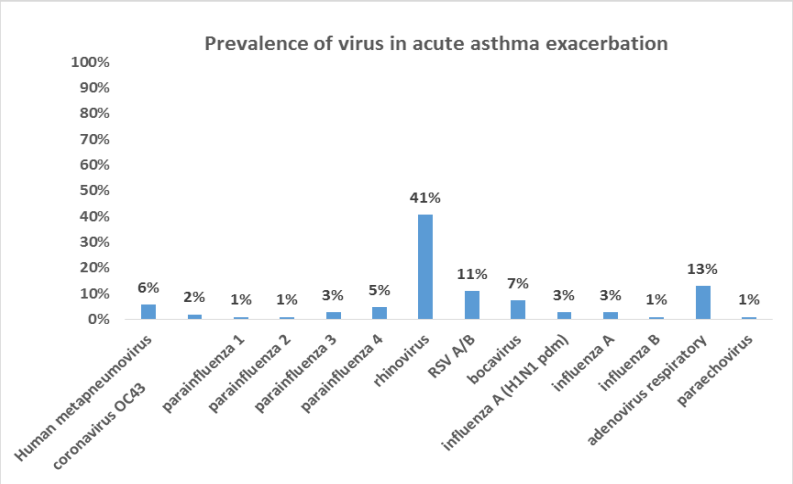
Viral infection

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positive	82	75.9	75.9	75.9
	Negative	26	24.1	24.1	100.0
	Total	108	100.0	100.0	

Respiratory viruses detected

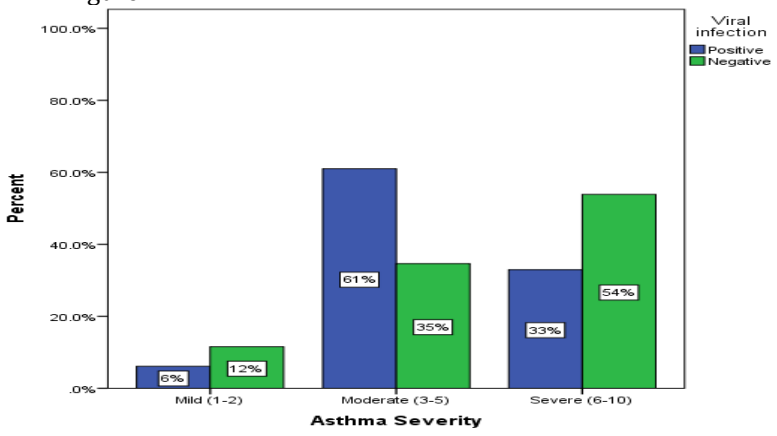
Respiratory viruses were detected in 82 (76%) of 108 sputum samples. Rhinovirus is the most frequently detected virus (41%), followed by adenoviruses (13%), RSV (11%), boca virus (7%) and human metapnumovirus (6%). (Table 3).

Table 3:



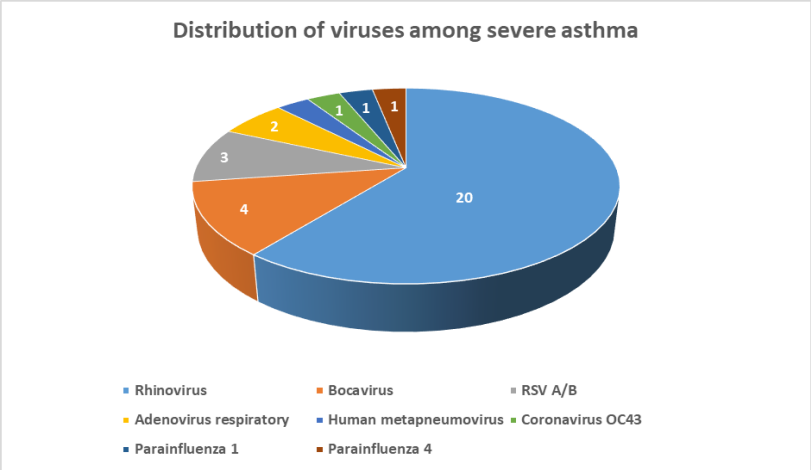
All patents who is admitted in the hospital during acute asthma exacerbation were classified into three group according to asthma severity. We compare between the presence of virus and the severity of asthma episode. Most of patients who had severe asthma course found not to have viral infection 54% compare to 61% of patent who have moderate asthma who have viral infection. (Figure 1).

Figure 1:



The most common virus found in severe asthma exacerbation is Rhinovirus 20 %, then Bocavirus 14.8%, RSV 11.1%, and adenovirus 7.4%. (Figure 2).

Figure 2:



Moreover, we found that there is no association between asthma severity and presence of virus. p value 0.062. No significant difference in severe asthma exacerbation with or without viral infection, 32.9% vs 53.8% accordingly, p value 0.055. (Table 4).

Table 4:

Viral infection * Asthma Severity Crosstabulation

			Asthma Severity		
			Mild (1-2)	Moderate (3-5)	Severe (6-10)
Viral infection	Positive	Count	5	50	27
		% within Viral infection	6.1%	61.0%	32.9%
		% within Asthma Severity	62.5%	84.7%	65.9%
	Negative	Count	3	9	14
		% within Viral infection	11.5%	34.6%	53.8%
		% within Asthma Severity	37.5%	15.3%	34.1%
Total		Count	8	59	41
		% within Viral infection	7.4%	54.6%	38.0%
		% within Asthma Severity	100.0%	100.0%	100.0%

Among the positive viral group, we compare the effect of virus and the severity of the episode. We found that Adenovirus has significant association with asthma severity. P value 0.021%. (Table 5)

Table 5:

Virus (positive)	Asthma Severity			
	Mild	Moderate	Severe	
	n (%)	n (%)	n (%)	p value
Human metapneumovirus	1 (16.7)	4 (66.7)	1 (16.7)	0.436
coronavirus OC43	1 (50.0)	0 (0)	1 (50.0)	0.106
parainfluenza 1	0 (0)	0 (0)	1 (100)	0.377
parainfluenza 2	0 (0)	1 (100)	0 (0)	0.540
parainfluenza 3	0 (0)	3 (100)	0 (0)	0.157
parainfluenza 4	0 (0)	4 (80.0)	1 (20.0)	0.399
Rhinovirus	1 (2.3)	22 (50.0)	21 (47.7)	0.074
RSV A/B	0 (0)	9 (75.0)	3 (25.0)	0.175
Bocavirus	0 (0)	4 (50.0)	4 (50.0)	0.457
influenza A (H1N1 pdm)	1 (33.3)	2 (66.7)	0 (0)	0.141
influenza A	1 (33.3)	2 (66.7)	0 (0)	0.141
influenza B	1 (100)	0 (0)	0 (0)	0.070
adenovirus respiratory	0 (0)	12 (85.7)	2 (14.3)	0.021*
Paraechovirus	0 (0)	1 (100)	0 (0)	0.554

*Statistically significant

We compare between different variables in both groups, with and without viral infection. Age of patients was spastically significant with presence of viruses, so the younger age the more likely to get viral infection. (P value 0.0001). The group of patients who have asthma exacerbation with viral infection is more tachypnic with respiratory rate around 55 breaths per minute, compare to the group who did not have viral infection with respiratory rate 45 breath per minute. Regarding Oxygen saturation on presentation, found lower with group who did not have viral infection around 88 %. The length of stay and the duration of Oxygen therapy was statistically not significant. (Table 6).

Table 6:

Variable		Viral infection Positive n (%)	Viral infection Negative n (%)	P value
Age, Mean±SD		3.77±2.29	6.19±2.67	0.0001*
Respiratory rate, Mean±SD		54.44±11.94	48.88±10.49	0.036*
Oxygen saturation, Mean±SD		91.41±4.48	88.58±5.64	0.010*
Oxygen therapy				
	Yes	56 (73.7)	20 (26.3)	0.468
	No	26 (81.2)	6 (18.8)	
Duration of oxygen therapy (days), Mean±SD		2.89±2.32	3.50±2.72	0.340
Length of stay, Mean±SD		4.48±2.33	5.00±3.26	0.369
Sex				
	Male	55 (72.4)	21 (27.6)	0.224
	Female	27 (84.4)	5 (15.6)	
Bed				
	Normal	44 (77.2)	13 (22.8)	
	HD	31 (77.5)	9 (22.5)	0.627
	PICU	7 (63.6)	4 (36.4)	
Corysal symptoms				
	Yes	82 (77.4)	24 (22.6)	0.056
	No	0 (0)	2 (100)	

Discussion

Although many studies have investigated the connection between viruses and asthma, few studies have focused on the relation between viruses and severity of asthma episodes. Here, we investigate the prevalence of certain viruses in asthmatic children's during acute asthma exacerbation and identify any correlation between certain virus and severity of the episode.

In this study we use of reliable method for detecting respiratory viruses. Previous reports indicate that the PCR method can be used to detect common respiratory viruses with both good sensitivity and good specificity [7] and they recommend it as the first choice for clinical diagnosis. Therefore, we used PCR for respiratory virus detection in this study [8,9]. Other important factors in the asthma exacerbation induced by respiratory viruses are the identity and viral species involved. A variety of viruses might be involved in the exacerbation of asthma. Several reports showing that viral infection is an important trigger for asthma exacerbation included only five or six viral species [10]. Here, we aimed to include as many respiratory viruses as possible; we detected 14 different viral species in our samples. In our study, the most commonly detected viruses in our study were Rhinovirus (41%), followed by adenoviruses (13%), RSV (11%), boca virus (7%) and human metapnumovirus (6%).

Asthma patients are predisposed to infections with respiratory viruses because the epithelia damage caused by uncontrolled asthma makes them more susceptible to these infections [11]. The use of ICS can restore intact epithelia and reduce the incidence of respiratory viral infections [12].

The impact of viral infection on asthma exacerbation remains an important issue. Interestingly, there have been reports that viral infections interact with allergen exposure in triggering asthma exacerbation [13]. Duff et al reported that the co-existence of high IgE levels and rhinovirus infection increased the risk of asthma exacerbation with an odds ratio of 10.8 [14].

Allergen exposure may increase the expression of intercellular adhesion molecule-1, which is the cell surface receptor for rhinovirus and facilitates its entry [15]. However, rhinovirus infection has been shown to promote airway hypersensitivity and eosinophil, neutrophil, and lymphocyte inflammation in an ovalbumin-sensitized mouse model [16]. A study by Message et al found that rhinovirus infection in an asthma patient increased both his asthma symptoms and airway eosinophil inflammation [17]. However, in our study, the most common virus found in severe asthma exacerbation is Rhinovirus 20 %, then Bocavirus 14.8%, RSV 11.1%, and adenovirus 7.4%. But Adenovirus has significant association with asthma severity. P value 0.021%. In general, there were no significant difference in severe asthma exacerbation with or without viral infection, 32.9% vs 53.8% accordingly, p value 0.055.

Conclusions

Respiratory viruses were identified in 75.9% of patients with acute asthma exacerbation. Rhinovirus is the most frequently detected virus (41%), but adenovirus has significant association with asthma severity (P= 0.021%). In general, there were no significant difference in severe asthma exacerbation with or without viral infection. p value 0.055

Disclosure

The authors declare no conflict of interest. No funding was received for this study.

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We acknowledge all hospital staff who contributed to this project.
Authors' contributions:
[1]BD and [2]HM participated in designing and developing the study, data collection, data entry, descriptive analysis of the data and witting up of the manuscript.
[3]YB supervised and help in conducting this research in all steps from writing the proposal up to writing the manuscript.

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