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Six-month to 3-year follow-up of children with acute respiratory infections caused by respiratory syncytial virus

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Abstract

Background and Objective: This study was performed to investigate long-term complications of Respiratory Syncytial Viral infections in patients admitted to Ali Asghar Hospital with acute respiratory infections who presented to follow-up outpatient clinics 6 months to 3 years after discharge, between years 2009 and 2011.

Methods*:* In this retrospective observational study that was performed in a descriptive cross-sectional manner, all patients suffering from acute bronchiolitis diagnosed with Respiratory Syncytial Virus, whose diagnosis had been confirmed by RCP of pharyngeal secretions, were included in the study. Data collection was performed through patient file reviews and questionnaires in outpatient clinics between 6 months and 3 years following discharge. Data collection included demographics such as age, sex, and address. Clinical data included inpatient documentations such as history of Atopic Dermatitis or Gastro-esophageal Reflux, or length of stay in Intensive Care Unit (ICU); and follow-up findings such as recurrent wheezing.

Results*:* Forty patients were included in the study, thirty-five percent of whom were male and 65% female; their average age was 33.6 months (SD: 12.08). The percentage of patients living in urban areas was 92.5%, with 65% living in Tehran. In the follow-up period of 6 months to 3 years, recurrent wheezing was recorded in 15%, pulmonary hypersensitivity in 40%, food allergy in 27.5%, exposure to cigarette smoke in 44.1% and enrolment in child day care facilities in 35% of the cases. In this study, there was no significant correlation between recurrent wheezing and factors such as age, sex, residence in Tehran, history of pre-term birth, length of stay in ICU, re-admission to hospital or exposure to cigarette smoke. There was a significant correlation between recurrent wheezing and atopic dermatitis and food allergy ($p< 0.05$).

Conclusion*:* In previous studies, Respiratory Syncytial Virus had been connected to complications such as recurrent wheezing; in this study, about 15% of patients followed up between 6 months and 3 years of discharge from hospital were found to have recurrent wheezing; there was a correlation between incidence of recurrent wheezing and factors such as atopic dermatitis or food allergies. Larger or multi-central studies are recommended to investigate long-term complications of RSV infection and their relationship with other predisposing factors.

Keywords: Acute Respiratory Infection, Respiratory Syncytial Virus, Recurrent Wheezing

Introduction

Acute respiratory infections are one of the major causes of mortality in children of under 5 years in developing countries; it accounts for about 33-50% of cases (1-3) In developed countries, viral infections such as those caused by Respiratory Syncytial Virus (RSV), adenoviruses, influenza and parainfluenza, and recently human metapneumovirus are the most common causes of lower respiratory tract infections (3-5)

RSV is the most common cause of lower respiratory infections among the viral causes (6). RSV is spread all over the world and each year, emerges as epidemics. In more temperate climates, RSV epidemics occur during winter and lasts for 4 to 5 months. RSV prevalence overlaps

with influenza and human metapneumovirus, and the rate of hospital admissions due to RSV is about 1-3%, largely due to acute bronchiolitis. Male to female ratio of RSV bronchiolitis and pneumonia is 1.5:1 (7).

In a study conducted in Hong Kong, annual incidence of RSV was estimated at 2-5/1000 with 0.15% mortality; with regards to the cost and hospital admission expenses consequential to RSV infections, vaccination against RSV is recommended (8). A previous study of ours investigated 158 hospital admissions due to respiratory distress with evidence of viral etiology; most of the cases of RSV infection occurred during winter and spring months, and RSV was isolated in 31% of the tested samples (9). Clinical manifestations of RSV infection were shown to be similar to those of metapneumovirus infection, but the average age of RSV infection is significantly lower (10). A Jordan study also showed that medical and financial burden of RSV infection in hospitalized infants have been sufficiently high to justify preventive measures such as vaccination (11). Several studies about viral infections have been conducted in Iran, including a study in Mazandaran that showed 54% of patients presenting with acute lower respiratory infections suffered from a viral etiology, where RSV was the second most common cause (12).

Some other studies described different factors to be considered in following up acute respiratory infections caused by RSV; for example, it has been shown that pre-term newborns with RSV infection have had a higher risk of developing recurrent wheezing or asthma in a 1-year follow-up program (13).

On the other hand, it has been shown that children with non-RSV acute respiratory infections have had a higher rate of hospital admissions as well as recurrent wheezing, in a 3-year post-admission follow-up program (14). However, severe bronchiolitis caused by RSV has been considered an important risk factor for recurrent wheezing and for hypersensitivity to common allergens up to 1 year after RSV infection (15).

Having considered the above-mentioned long-term complications of RSV infection, and having noticed paucity of evidence in this field in our country, the authors initiated this study to follow up patients with RSV infection for a 6-month to 3-year post-discharge period, to document complications such as recurrent wheezing, atopic dermatitis, food allergies and otitis media. As there have been few epidemiologic studies of this context in developing countries, especially in Iran, and because of the significant financial burden of RSV infections, even long after discharge from hospital, conducting such studies are well justified; results from such studies could at least provide educational materials for the families hit by RSV, to minimize potential complications and therefore reduce further medical and financial burden.

Methodology

In this descriptive cross-sectional study, all patients admitted to Ali Asghar Pediatric Hospital with final diagnosis of RSV bronchiolitis, were included. The inclusion criteria were defined as infants with acute respiratory infection, whose general condition, baseline lab tests (CBC, diff, ESR) and chest X-ray indicated viral bronchiolitis as the most likely diagnosis, and whose RSV PCR test proved positive. The exclusion criteria were defined as reluctance of the attending physician in including the patient, or refusal to consent by the patient's parents or guardians. The study was ethically confirmed by the Azad University Ethics Committee and confidentiality was respected through all the stages of the study.

Patients were recalled for follow-up visits, during which a questionnaire was handed in to the parents to fill in during the appointment. All the patients were followed up at least 6 months up to 3 years. The collected data was analysed by SPSS version 13; for qualitative variables, variance and percentage of variance were considered; for quantitative variables, mean and standard deviation were measured. Correlations were tested by chi-squared, Fisher's exact, and independent t-test, with a significance value of less than 0.05%.

Findings:

Forty patients were included in the study 35% of whom were male; average age of the patients was 33.6 months with a standard deviation of 12.08 months.

Average number of family members was 4 (SD: 0.84). Average age of starting food supplements was 6 months (SD: 1.05). Average length of ICU stay was 7 days (SD: 5.16). In 5.9% patients the parents were blood relatives. The percentage of patients living in urban areas was 92.5%. Fifteen percent of patients were orphanage residents. Infants of term delivery constituted 64% of the cases; birth weight was low in 17.6%, normal in 79.4%, and high in 2.9% (macrosomia, birth weight of over 4000 grams). Current or past atopic dermatitis was present in 5%, and family

history of eczema was reported in 26.5% of the patients. There was a history of past or current congenital heart disease in 12.5% of the cases, while 55% suffered from gastro-esophageal reflux. Previous hospitalisation was reported in 22.5% of patients. Ventilator use was required in 30% of the cases.

Post-discharge findings were single episode of wheezing in 35%, recurrent wheezing in 15%, and chronic cough of more than 3 weeks or nocturnal or diurnal cough of more than twice a week in 25% of the cases. At discharge, food allergy was reported to be present in 27.5% of the patients, and 52.5% were breast fed, while 27.5% were given formula milk with cow's milk base; and 20% took hypo-allergenic formula milk. In this study, there was a reported exposure to cigarette smoke in 44.1% of the cases.

There was a re-admission rate of 25% among the study group, with the cause of re-admission being respiratory disease in 50%, cardiac disease in 30% and other causes in 30%. Regarding compliance with treatment, about 42% regularly took their medications, the most common of which was Salbutamol (70%). A third of the patients attended day care nurseries; there was a 42% incidence of recurrent otitis media reported in discharged patients. The height and weight of the patients was normal in 95% and 82.5% of the cases, respectively.

With statistical analysis of the data, the findings were a correlation between recurrent wheezing and food allergies (P= 0.02); and between recurrent wheezing and atopic dermatitis (P= 0.039). Children residing at orphanages were examined more closely with the results shown in Table 1.

Discussion

The results of this study shows that RSV plays a major role in etiology of recurrent wheezing; this has previously been mentioned in studies such as Henderson et al (16), in which RSV was viewed as the most important factor in causing recurrent wheezing. Besides the descriptive report in our study, there were similar findings to previous studies, but with no statistical significance; this could be due to our relatively small study volume; for example, there was no significant correlation of age and gender with recurrent wheezing (P> 0.05). The average age of patients was 33.6 months (SD = 12.08), which was similar to the study by Garcia et al (17). Average number of family members in patients was 4 (SD = 0.84) that could imply the population density of the family; in Colosia et al (18), larger number of family members was considered a risk factor for RSV infection. In our study, like Hosoki et al (19) the number of family members showed no significant correlation with recurrent wheezing. In studies such as Ermers et al (20), patients' genetic map, especially in pathogens causing recurrent wheezing, was taken as a good predictive factor; however, close family relationship had no significant correlation with recurrent wheezing in our study.

In our study, there was no significant correlation between residence in Tehran and recurrent wheezing. Although it was expected that air pollution influence intensity and chronicity of long-term complications such as recurrent wheezing, there was no correlation; this could, of course, be due to the above-mentioned limitations in our study, such as being descriptive, having a small study volume, and limitations in the follow-up center. There was no significant relationship between residence in orphanage and recurrent wheezing, but the small number of our sample could be a limiting factor. The study showed that 64.7% of the patients have been the product of term delivery, which again proves no correlation between recurrent wheezing and term or pre-term labor, although in previous studies (21), pre-term labor has been considered as a risk factor for recurrent wheezing; however, Hosoki et al (19) have considered pre-term labor as unrelated to recurrent wheezing. Breast feeding was recorded in 52.5% of the patients, whereas 27.5% took cow-milk based formulas and 20% fed on hypo-allergenic formulas, quite similar to previous studies. Low birth weight, which has been a known risk factor in previous studies, was present in 17.6% our cases; this means that there was no significant relation with this factor either;

Table 1. Distribution of the qualitative variables in children residing at orphanage.

	Asylum	Mean	Std. Deviation
Age (mo)	Pos	32.33	14.208
	Neg	33.82	11.907
Supplementary Feeding Month	Pos	6.00	.000
	Neg	6.03	1.141
ICU Stay Duration (days)	Pos	6.75	2.363
	Neg	7.22	5.543
Disease Initiation Age (mo)	Pos	3.33	1.211
	Neg	6.29	3.224

The average age, age at start of food supplements, length of hospital admission, and age at infection were all higher in non-orphanage children (P= 0.05) except for the last item.

the same findings were true with Hosoki et al (19). Congenital heart disease was found in 12.5% of our cases, unlike the reported 20% in previous studies (22); this means there was no significant relation between congenital heart disease and recurrent wheezing.

The recurrent wheezing relationship with atopic dermatitis was shown to be significant. Atopy in general, including dermatitis and ophthalmic involvement, had a significant coincidence with recurrent wheezing; according to Tian et al (23), atopy is a significant risk factor for recurrent wheezing. In our study, as mentioned before, recurrent wheezing was present in 50% of cases, in whom 15% was repeated; the relationship between allergic diseases and RSV infection was the same as previous studies (24). In a study conducted by Kafentzis et al (25) in a 6-month follow-up of infants less than 2 years of age who had been hospitalized due to RSV infection, incidence of otitis media was investigated. RSV played an important role in causing otitis media in hospitalized patients. Those hospitalized had a 32.5% incidence of otitis media, with 46.2% suffering recurrent infection; this shows a relationship between otitis media and RSV infection.

There was also a significant relationship between recurrent wheezing and food allergy. Food allergy was present in 27.5% of cases; with regards to previous studies (24) reporting the same relationship, this was a significant finding.

Residence in orphanage was reported in 15% of our cases, whose average age was lower than that of non-orphanage residents; this could be due to more exposure to RSV and more crowded conditions; however, we did not find any significant correlation. In fact, Hosoki et al (19) had shown, with their 99 cases of hospitalization with RSV infection, that some host factors susceptible to wheezing and chance of infection due to attending a daycare may be related to recurrent wheezing; this may require further studies in orphanages with a larger study sample.

In 44.1% of cases, exposure to tobacco smoke was reported, and according to Defranz et al (26) is in itself a major risk factor for intensity of RSV infection; we could not find a significant relationship with this factor. Re-admission was necessary in 25% of our patients, whose reason for hospitalization was respiratory diseases in 50%; this also is consistent with the previous studies.

Conclusion

We can conclude that Respiratory Syncytial Virus is the most important factor in causing recurrent wheezing related to allergic conditions, such as the previously-proved atopic dermatitis and food allergy. According to the results of the study, we suggest future studies investigate the efficacy of the parental education, allergy control, and especially preventive measures regarding food allergy, to reduce the incidence of RSV bronchiolitis and its complications. We also suggest larger studies with multi-central sampling, and on other viruses such as human metapneumovirus, be conducted, so that more is known about long-term complications of such viruses and about the environmental factors influencing such complications.

Conflicts of interest: None declared.

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