

## The Incidence of RSV Infection in the Cases Hospitalized with Bronchiolitis Diagnosis and the Relevant Clinical Particulars

Vefik Arica<sup>1\*</sup>, İbrahim Şilfeler<sup>2</sup>, Hatice Onur<sup>3</sup>, Hüseyin Dağ<sup>3</sup>, Sayat Gülbayzar<sup>3</sup> and Ömer Obut<sup>4</sup>

<sup>1</sup>Mustafa Kemal University Medical Faculty, Pediatric Clinic, Hatay, Turkey

<sup>2</sup>Okmeydanı Training and Research Hospital, Pediatric Clinic, MD, Istanbul, Turkey

<sup>3</sup>Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Pediatric Clinic, MD, Istanbul, Turkey

<sup>4</sup>Istanbul Training and Research Hospital, Anesthesiology Clinic, MD, Istanbul, Turkey

### Abstract

**Aim:** This study aims to investigate the incidence and clinical particulars of Respiratory Syncytial Virus (RSV) infection in infants hospitalized with bronchiolitis diagnoses between the years of 2006 and 2009.

**Material and method:** From October 2006 to October 2009, the registers of a total of 112 patients (< 2 years old) who were diagnosed with bronchiolitis and for whom RSV antigen was scanned in the nasopharyngeal swab sample were screened retrospectively and their clinical and laboratory particulars were evaluated. RSV antigen was sought through the enzyme immunoassay method by using Respi-Strip RSV (Coris Bioconcept).

**Results:** RSV infection was detected in 31 (27.6%) cases. The families of the RSV-positive patients were larger and their parents were older. The CRP positivity of RSV-positive cases was of a higher rate than that of RSV-negative patients. RSV infection was most frequently detected in January. The rate of hospitalization and treatment of RSV-infected infants in the intensive care unit was statistically and significantly higher than that of the RSV negative patient group.

**Conclusion:** We have detected a high rate of RSV infection in the cases hospitalized with bronchiolitis diagnosis, which is in line with the literature. The detection of RSV infection in these patients will prevent unnecessary antibiotic. In addition, virus-related hospital infections will be controlled more easily.

**Keywords:** Bronchiolitis; Respiratory syncytial virus; Infant

### Introduction

Respiratory Syncytial Virus (RSV) which is a RNA virus from the paramyxovirus family retaining the ciliary epithelial cells of respiratory tracts is the most significant reason of viral Lower Respiratory Tract Infection (LRTI) in infants and young children, such as pneumonia and bronchiolitis [1]. It is reported that all children have experienced RSV infection at least once before the age of two, while 10-20% have been infected by the virus more than once before that age [2]. The incidence of RSV in respiratory tract infections has been reported as 11-51% in different studies in our country [3-6]. The virus enters the host through the host's direct contact with large droplets and secretions containing the virus. According to data obtained from the World Health Organization (WHO) 10.5 million children under the age of two lose their lives every year due to preventable and treatable diseases. Lower respiratory tract infections are held accountable for 28% of these mortalities [7-9].

The incidence of diseases related to respiratory syncytial virus is seasonal. The studies conducted in our country report that the incidence is seen between November and April, most notably in December and January [5,10-12]. Antigen detection in nasopharyngeal secretion is the recommended method of diagnosis during the disease period. This test is more precise for adult patients due to the longer and more intensive spread of virus in infants [1]. The use of viral culture is not practical. Respiration support and hydration are basic treatments for the respiratory syncytial virus infection [13]. Due to the absence of efficient treatment and vaccination for respiratory syncytial virus, protection is recommended for the high-risk patient group with RSV IVIG and RSV monoclonal antibodies in order to provide protection against RSV infections [14,15].

This study evaluates RSV incidence in etiology, and its clinical and laboratory particulars in our patients diagnosed with bronchiolitis in concurrence with literature.

### Material and Method

In October 2006-October 2009, a total of 672 patients were monitored with LRTI diagnosis in the Children's Polyclinic, Children's Service and Intensive Care Unit. The registers of the cases for which RSV was examined in the nasopharyngeal swab samples were screened retrospectively and 112 children under the age of 2 years with bronchiolitis were enrolled in the study. The patients who were brought in with complaints of fever, coughing, wheezing, rustling and difficulty breathing were diagnosed with bronchiolitis through the lengthiness of their expirations, the detection of coarse noises and X-ray findings.

Information about the patients was obtained from their registers and include age, gender, pregnancy weeks, date of application, duration of nutrition with breast milk, history of atopy in the family, body temperature, admission term of hospitalization, need for respiration support and laboratory results. It was observed that RSV examinations were required for the patients with clinical and laboratory findings that were suggestive of viral infection. The cases with proven bacterial infection were not enrolled in the study. None of the patients previously received prophylactic treatment for RSV. Sample collection from the patients was performed with a nasopharyngeal swab, nasopharyngeal irrigation or closed system nasopharyngeal aspiration for the RSV

**\*Corresponding author:** Vefik Arica, M.D., Medical Faculty of the Mustafa Kemal University 31100, Serinyol, Antakya, Hatay, Turkey, Tel: +90 326 2291000; Fax: +90 326 2455654; Mobile: +90 505 6797877; E-mail: [vefikarica@hotmail.com](mailto:vefikarica@hotmail.com)

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test. Nasopharyngeal swab samples were analyzed with the rapid immunochromatographic membrane method (Respi-Strip RSV, Coris Bioconcept) within 30-60 minutes of sample collection in the Microbiology Laboratory. Following the verification of positive and negative controls the results obtained from the patients were evaluated in each operation periods of the kits.

The statistical analysis was performed with a SPSS 15.0 program during the evaluation of the data obtained from the study results. The data was provided as mean  $\pm$  SD (standard deviation). Qualitative data were compared with the chi-square test and the student *t* test. Statistical significance was established as  $p < 0.05$ .

## Results

A total of 112 patients, 61 of which are female and 51 of which are male were enrolled in the study. The participants' ages were in the range of 0-24 months. The mean age of the children was RSV (+)  $4.4 \pm 2.8$  months, RSV (-)  $6.1 \pm 4.7$  months. Thirty one (27.6%) patients were RSV-positive, and 81 (72.4%) patients were RSV-negative. Respiratory syncytial virus positivity was found in 14 female and 17 male patients, whereas there were 44 female and 37 male RSV negative patients. Within the study group, RSV infection was found in a total of 8 babies out of 19 who were born earlier than week 36 of the pregnancy (i.e. 5 out of 11 babies who were born within weeks 27-32 of pregnancy, and 3 out of 8 babies who were born within weeks 33-35 of pregnancy). The average age of RSV positive patients and the average age of pregnancy were  $4.4 \pm 2.8$  months and  $36.4 \pm 3.8$  weeks, respectively; the average age of RSV negative patients and the average age of pregnancy were  $6.1 \pm 4.7$  weeks, and  $37.0 \pm 3.1$  weeks, respectively. The average age of RSV positive patients and the average age of pregnancy were less than those of the RSV negative group however, this difference was not found as statistically significant ( $p=0.32$ ). No significant difference was established between RSV positive and negative cases in respect to gender, presence of social security, vaccination status, education level of the parents and their smoking status ( $p=0.24$ ). The comparison of RSV positive and negative patients is summarized in Table 1 as per sociodemographic properties and laboratory findings.

The siblings count of RSV positive children was significantly higher than that of RSV negative children ( $p=0.02$ ). The average age of the parents of RSV positive children (mothers  $36.9 \pm 7.6$  years; fathers  $42.4 \pm 10.8$  years) was significantly higher than the age of parents of RSV

negative children (mothers  $31.5 \pm 8.2$  years; fathers  $35.0 \pm 8.6$  years;  $p=0.02$ ).

The number of RSV positive patients within a time period of 3 years is as follows; 2 in October, 3 in November, 35 in December, 39 in January, 17 in February, 4 in March, 6 in April, 2 in May, 1 in June, 0 in July, 1 in August, and 2 in September (Figure 1). The average period of nutrition with breast milk was  $3.4 \pm 2.4$  months in the RSV positive group, and  $3.9 \pm 2.0$  months in the RSV negative group. History of asthma-atopy was found in 4 (12.9%) RSV positive patients, and in 13 (16.0%) RSV negative patients.

While nasal flow was observed in all of the RSV positive cases, this rate was found as 75.3% of RSV negative cases. A statistically significant relationship was established between RSV positivity and nasal flow ( $p < 0.05$ ). No significant difference was determined between the two groups in respect to clinical symptoms and findings, including coughing, wheezing, groaning, vomiting, apnea, dyspnea, conjunctivitis, and hyperemia in the tympanic membrane ( $p=0.31$ ). No significant difference was found with regards to the examination of findings of the respiratory system ( $p=0.46$ ).

The average body temperature at the time of application was measured as  $37.4 \pm 0.6^\circ\text{C}$  in the RSV positive group, and as  $37.3 \pm 0.4^\circ\text{C}$  in RSV negative group. The average leukocyte count was  $9.442 \pm 3.035/\text{mm}^3$  [3] in the RSV positive group and  $10.012 \pm 3.114/\text{mm}^3$  [3] in the RSV negative group. The average body temperature and levels of leukocyte count did not differ between the groups ( $p=0.14$ ). CRP values are higher in the RSV positive group. The positivity rate of CRP was 93.5% and 66.6% in the RSV positive cases and RSV negative cases, respectively.

Twelve (10.7%) patients were monitored with pneumonia + bronchiolitis diagnosis, and 73 (89.3%) patients were monitored with bronchiolitis diagnose. Hospitalization period was established as  $6.7 \pm 10.1$  days in the RSV positive group, and as  $3 \pm 4.2$  days in the RSV negative group. No statistically significant difference was found between RSV positive and negative patients with respect to hospitalization rates and periods ( $p=0.16$ ). Six (19.3%) patients from RSV positive and 4 (4.9%) patients from RSV negative group were hospitalized in the intensive care unit due to their need of advanced respiration support. All of these patients were babies younger than 6 months. The rate of hospitalization in the intensive care unit was statistically and significantly higher in RSV positive patients ( $p=0.01$ ).

	RSV(+) (n=31)	RSV(-) (n=81)	p
Age (months)	4.4 $\pm$ 2.8	6.1 $\pm$ 4.7	$p > 0.05$ ***
Sex			
Female n (%)	14 (%45,2)	44 (%54,3)	$p > 0.05$ ***
Male n (%)	17 (%54,8)	37 (%45,7)	
Average age of pregnancy (weeks)	36.4 $\pm$ 3.8	37.0 $\pm$ 3.1	$p > 0.05$ ***
Average age of mothers (years)	36.9 $\pm$ 7.6	31.5 $\pm$ 8.2	$p < 0.05$ *
Average age of fathers (years)	42.4 $\pm$ 10.8	35.0 $\pm$ 8.6	$p < 0.05$ *
Asthma-atopy history n (%)	4 (%12,9)	13 (%16)	$p > 0.05$ ***
Nutrition period with breast milk (months)	3.4 $\pm$ 2.4	3.9 $\pm$ 2.0	$p > 0.05$ ***
Body temperature ( $^\circ\text{C}$ )			
Leukocyte count (/mm <sup>3</sup> )	37.4 $\pm$ 0.6	37.3 $\pm$ 0.4	$p > 0.05$ ***
CRP (mg/dl)	9.442 $\pm$ 3.035	10.012 $\pm$ 3.114	$p > 0.05$ ***
Hospitalization period (days)	29 (%93,5)	54 (%66,6)	$p < 0.01$ **
Intensive care advanced respiration support n (%)	6.7 $\pm$ 10.1 6 (%19,3)	3 $\pm$ 4.2 4 (%4,9)	$p > 0.05$ *** $p < 0.05$ *

The values are presented as average  $\pm$  SD

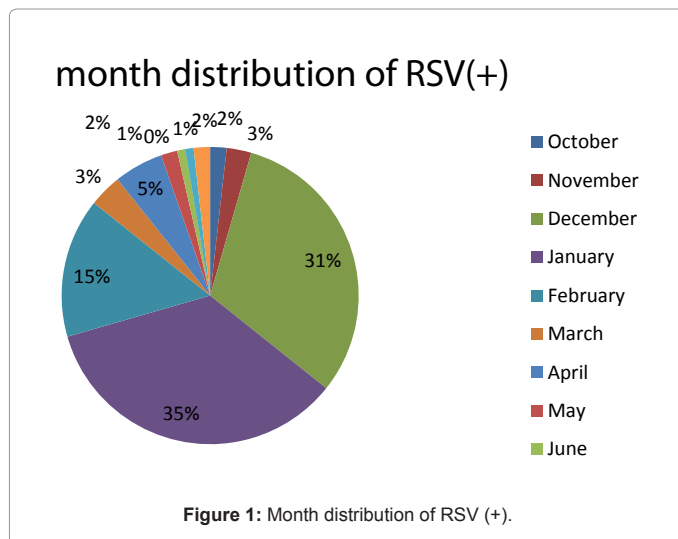
RSV: Respiratory Syncytial Virus

\* $p < 0.05$ : Statistically significant

\*\* $p < 0.01$ : Statistically highly significant

\*\*\* $p > 0.05$ : Statistically insignificant

**Table 1:** The comparison of RSV positive and negative patients as per sociodemographic properties and laboratory findings.



## Discussion

Lower respiratory tract infection is one of the infections that is seen among children worldwide with high morbidity and mortality rates. These infections are held responsible for the death of 4 million children, particularly under the age of 5, in developed and developing countries every year [1]. RSV is the common cause for lower respiratory tract infections, including bronchiolitis and bronchopneumonia in infants and young children, and it generally heals spontaneously and rarely leads to death in normal infants. However, rates of serious disease and mortality increase in infants and children with risk factors such as congenital heart disease, chronic liver disease, immunodeficiency, hypoxia, being younger than 6 weeks and birth prematurity [1].

In this study, RSV infection was found positive in 27.6% of our patients diagnosed with bronchiolitis. This rate is in accordance with publications previously reported in our country [3,6]. Forgie et al. [16] determined in a study that the rate of viral infections was 34% in children from 1-9 years of age who were hospitalized due to lower respiratory tract infection, and that RSV was the viral agent most frequently seen with a rate of 12%. Zeleya et al. [17] indicated RSV as the predominant reason for bronchiolitis in children hospitalized under the age of 1 year, and showed the virus in nasopharyngeal cells in 75% of the cases with bronchiolitis. Eriksson et al. [18] detected RSV infection by using direct immunofluorescent tests in 66% of 135 children under the age of 3 years with lower respiratory tract infection. In similar studies performed, the rates of RSV frequency found by Korppi et al. [19], Dereli et al. [20], and Saijo et al. [21] were 38.1%, 29.2%, and 28.9%, respectively. In our study, frequency of RSV positivity was detected as 27.6%. When compared to other studies, only RSV positivity detected by Zeleya et al. [17] was considerably higher (75%). We speculate that this highness is affected by the selection of our age group (0-1 years). We can tell that the frequency that we have found is of similar rates with the other studies.

RSV is an epidemic virus that spreads during specific periods of the year [22]. The cases are usually observed between December and April in mild temperate regions, and between June and December in tropical climate regions in which rain downfalls increase [23]. In our study, the cases have been seen mostly in January gradually decreasing and having nadir in July, which is in line with the literature. Infants who live in populous living conditions and who have elder sibling are at risk due to exposure to more frequent and more viral loads [23-25].

It has been detected that the RSV positive children have elder parents and more siblings in our study. Older siblings who come home from school can easily carry infections. However, this spread of infection can be reduced by hand washing.

Exposure to passive smoking is known to be a significant risk factor for lower respiratory tract infections [9]. The rate of smoking was found as 55% for the mothers, and as <70% for the fathers in our study. This is suggestive that smoking is a significant risk factor for our cases. However, no significant relationship was established between exposure to passive smoking and RSV detection. Nineteen (16.9%) patients who were enrolled in our study had premature birth history, and 8 (42.1%) of the premature patients were detected with RSV infection. This result was remarkable due to the fact that it indicated the significance of prophylaxis of those with premature birth history with RSV immunoglobulin. As for CRP positivity, CRP positivity was significantly more frequent in RSV positive cases. This supports the finding that acute phase reactants increase in RSV infections.

A large number of children are hospitalized due to RSV infection in every year. For example, approximately 91.000 children are hospitalized due to RSV infections in the U. S. A., where approximately 300 million dollars are spent for these children annually [26]. When a cost benefit analysis is done for the rapid diagnosis of the factors of viral respiratory tract infections, use of rapid tests in virus detection has been detected to be advantageous on several counts for the diagnose of respiratory tract infections. Rapid detection of viruses prevents unnecessary use of antibiotics, which can also develop resistant strains of bacteria to antibiotics, and directs the patients to more appropriate therapy with precise diagnosis, shortening the hospitalization periods of the patients [27]. The spread of the disease can be prevented by simple methods such as bringing the RSV patients into single rooms, dedicating the patients to a certain group of nurses, hand washing before and after contact with the patients, using overalls, gloves and protective masks, and limiting the entry and exit of visitors.

In consequence, RSV infection was detected at a high rate (27.6%) in the cases, between the ages of 0-2 years who were, hospitalized with the diagnosis of lower respiratory tract infection in line with the literature. The detection of RSV infection in these patients would ensure the prevention of the unnecessary antibiotic use, and virus-related hospital infections will be controlled more easily. Finally, antiviral treatment will be applied for the relevant patients.

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