Original Article

Clinico demographic profiling of the *Respiratory syncytial virus* (RSV) infected children admitted in tertiary care hospital in North India

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Abstract

Background: Acute bronchiolitis is fatal disease involving lower respiratory tract of infants and children of paediatric age group. Respiratory Syncytial Virus (RSV) is responsible for causing more than 70% hospital admissions of children aged less than 2 years thus making a necessity for accurate and timely diagnosis. **Aims:** The main aim of study was clinicodemographic correlation of RSV positive children presenting to our tertiary care hospital. **Setting and Design:** It is a retrospective study done between December to January 2018. **Materials and Methods:** Detection of RSV antigen from nasophyrangeal aspirates using Mouse Monoclonal anti RSV Antibody (by Novatetra) and Goat Anti Mouse Antibody conjugated with FITC as secondary antibody. **Results:** A total of 147 samples were received in the laboratory and 20 were tested as positive for RSV Antigen. Totally, 19/20 children were aged less than 1 year and with a male predominance. The most common symptom was cough and respiratory distress. Eight percent of the children showed wheezing and 18/20 required assisted ventilation. The clinical course in one child deteriorated leading to death of that patient. **Conclusions:** The timely diagnosis and management of RSV infected children is utmost needed to prevent morbidity and mortality. The premorbid conditions can assist to differentiate the viral from bacterial pneumonia and thus enable speedy recovery of the child.

Keywords: Bronchiolitis, croup, pneumonia, respiratory syncitial virus, RSV

Introduction

Acute respiratory tract infections (ARIs) rank second amongst the leading causes of childhood deaths with approximately 70% of these infections occurring in Africa and Southeast Asia.[1] Human Respiratory Syncytial Virus (RSV) is a causative agent of severe viral respiratory tract infection worldwide leading to >80% of LRTI cases. The main outcome of RSV infection is bronchiolitis which is responsible for numerous hospital admissions of children less than five years.[2] The disease course of bronchiolitis is found have a variability and the disease dynamics differ in different individuals, with transient episodes of apnoea, progression to respiratory distress and causing obstruction of lower respiratory tract in severe cases. Majority of the cases are benign, taking 3-5 days for recovery, but in patients with co-morbid conditions like underlying chronic lung diseases and congenital heart disease, the infection leads to a fatal course with clinical worsening.[3]

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The other viruses apart from RSV in causing acute LRTI are, *Parainfluenza; Adenovirus; Rhinovirus; Mycoplasma* and emerging viruses like *Human metapneumovirus* and human *Boca virus*.[4-6] A distinct seasonal distribution has been observed in outbreaks, which is commonly seen in earlier months of the year in temperate and Mediterranean climates and during wet season in tropical climates.[7] The clinical details were obtained retrospectively from records to look for their demographic, clinical, haematological profiles whose nasopharyngeal aspirate samples were received in our laboratory to rule out RSV bronchiolitis. This study has emphasised the need to correlate symptoms of patients with the various clinicodemographic characters so as to catch the cases early and start effective management even before the diagnosis is made.

Material and Methods

The study involved children aged less than 10 years of age attending the hospital between January to December 2018, whose nasophyrangeal aspirates were received for viral diagnosis in the Department of Virology of PGIMER Chandigarh. The samples received were subjected to RSV antigen detection using Mouse Monoclonal anti RSV Antibody (by Novatetra) and Goat Anti Mouse Antibody conjugated with FITC as secondary antibody. Ethical Approval obtained on 24/06/2020 vide letter number INT/IEC/2020/SPL-773.

Results

A total of 147 samples were received in viral serology laboratory of PGIMER Chandigarh over one year period (January 2018-December 2018) for RSV antigen testing and out of them, 20 (13.6%) came out to be positive for RSV antigen. Totally, 19 out of 20 (95%) of patients were aged less than 1 year with male to female ratio of 14:6. The mean age of the RSV positive children was approximately 9 months.

The most common symptom in RSV positive group was respiratory distress (20/20) followed by cough (100%), fever 17/20 (85%), cold 15/20 (75%), nasal discharge 15/20 (75%), vomiting in 8/20 (40%). Meningitis was seen in 3 patients out of which one had disseminated RSV and the other two had a severe disease course. Only two patients had seizures. Birth history of RSV positive revealed that 70% (14/20) patients had low birth weight with a mean weight of 1.98 kg whereas, 30% (6/20) had complicated delivery. Three out of 20 had NICU admission after birth.

Physical examination revealed that 17/20 (85%) children were small for age and height. Totally, 16/20 (80%) had nasal flaring. 85% (17/20) children had subcostal retraction and 14/20 (70%) had intercostal retractions on examination. Tachypnea was seen in (15/20) 75% of children. Wheezing (16/20) and crepititions (15/20) were present in 80% and 75% patients, respectively. 25% of children developed acidosis during the illness leading to CO2 retention and hyperinflation of lungs thus complicating their illness and requiring prolonged ICU stay. 1 patient died due to ARDS. 18 out of 20 patients required assisted ventilation. Haematological profiles showed 65% (13/20) children to be anaemic with a mean haemoglobin concentration of 9.8. 65% (13/20) had a raised total leukocyte count. 58% of children had raised lymphocyte count. 16 out of 20 patients had a low calcium concentration in blood. CRP report was available for only 17 patients of which 13 patients had raised value. Similarly of 18 patients whose procalcitonin report was available 15 had raised procalcitonin levels. Out of 18 patients whose Liver function tests reports were available, 17 had high AST whereas 11 had raised levels of ALT. Only 3 patients had a raised ALP levels.

Discussion

Acute bronchiolitis is an important cause of morbidity in infants and young children. It has been recognised as one of the most important reasons for hospitalisation of children of all age group (particularly <5 years) presenting with acute LRTI. Through this retrospective study, the authors have tried to highlight the clinical features, haematological parameters, sociodemographic characters of infants and children admitted to our hospital presenting with acute bronchiolitis.

RSV has been recognised as an important cause of LRTI that is, bronchiolitis, pneumonia and sometimes croup, especially in children less than one year.[8] The typical age group involved in RSV bronchiolitis is between 2 to 6 months of age.[3] A study from Cameroon mentioned in their study that RSV is major cause of ARI in children aged less than 6 months.[9] Various studies estimated that around 95% of the children have already been infected with RSV till they reach 2 years of age.[10] Majority of the deaths caused due to RSV has occurred in developing countries. It commonly occurs as an epidemic during winter season.[11] A seasonal association with the symptomatic and demographic profile, (as cases are often in close knit areas and the presentation is almost similar) can guide a clinician to come to an early diagnosis and hence decrease in mortality associated with disease. Henshaw *et al.* has emphasised in their study the importance of an effective RSV surveillance system for public along with standardised laboratory equipment and techniques for better understanding of RSV disease, incidence, seasonality, disease burden among patients.[9] They have also emphasised the role of primary and secondary health care givers to make an early diagnosis as per the symptomatology to aid in infection control and diagnosis.[9] This applies to developing country like India too where people are not able to approach facilities and the primary decision relies on health care giver who primarily comes in contact with the patient.

Presently, majority of infected children (19/20) were less than 1 year age [Table 1] with mean age of 9 months with a predominance male children also observed by Syed *et al.*[12] Radhakrishnan *et al.* reported a median age of 9 months.[13] Thomas *et al.* also observed male predominance (51%) over

Table 1: Demographic and clinical feature of patients

TABLE 1- DEMOGRAPHIC AND CLINICAL FEATURES OF PATIENTS		
Demographic features	**Number(n)**	**Percentage(%)**
Age distribution(n=20)		
1mo- 6mo	14	70
7 mo- 1 year	5	25
>1year-1.5 year	0	0
>1.5 year	0	0
2 year- 2.5 year	1	5
>2.5 year	0	0
>3year	0	0
Sex(n=20)		
Males	14	70
Females	6	30
Delivery at term (n=20)		
Preterm	5	25
Post term/term	15	75
Low Birth Weight	15	75
Place(n=20)		
Punjab	10	50
Haryana	4	20
Chandigarh	4	20
Himachal Pradesh	1	5
Uttar Pradesh	1	5
SFA(n=20)		
No	3	15
Yes	17	85
Clinical features(n=20)		
Symptoms		
Respiratory distress	20	100
Cough	20	100
Fever	17	85
Cold	15	75
Nasal discharge (75%)	15	75
Vomiting (42%).	8	40
Meningitis	3	15

females (49%).[14] Saleh Ahmed conducted a retrospective study involving 70 children with RSV bronchiolitis and found out a male predominance with children aged <6 months being infected majorly.[15] Durani *et al.* showed the mean age of 5 months with a male predominance (57%) in his prospective cohort study.[16] Radhakrishnan *et al.* also reported a male predominance (63.8%) in their study.[13] RSV infection occurs worldwide, especially during the winter months, and majority children are infected till they reach age of 2 years, but, lower respiratory tract symptoms develop in only 40% of them.[17,18] Presently also, cases presented in winter months that is from November to March. [Figure 1]

Studies have shown an association of pre-morbid conditions leading to an increased severity of RSV infection.[6,19,20] Of this premature birth has been identified as one of the most important factor. In our study 25% (5/20) children were born prematurely which is identical to the Canadian study in which 20% of cases were born premature.[21] A premature infant has a lower number of alveoli and thus, decreased anatomic barriers to gas exchange, which leads to increased lethality associated with bronchiolitis and any pulmonary infection.[19] It is also seen that transfer of maternal *IgGs* (protecting against RSV infection) occur at the latter part of gestation, therefore, increasing the risk of RSV infection in the premature infants.[22] In our study 15/20 (75%) children had low birth weight which is also a factor seen to be associated with development of RSV infection. An observational cohort study also known as PICNIC study was conducted in Canada which identified various independent predictors of

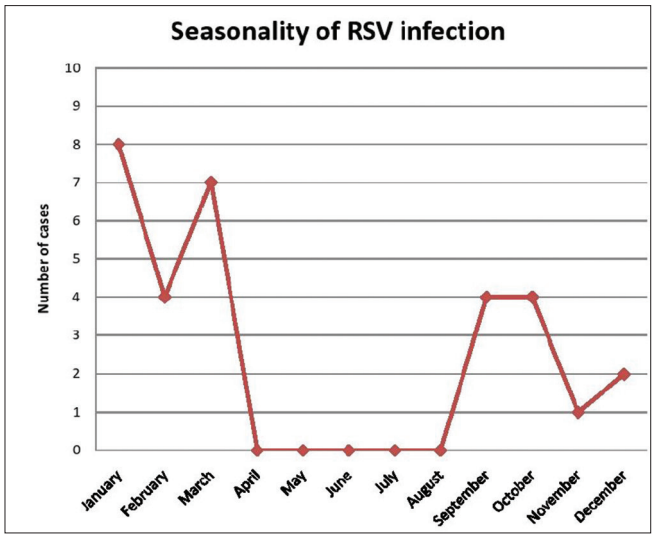

Figure 1: Seasonality of RSV Infection

increased risk of RSV- hospitalisation in children that is, birth during first half of RSV season (November-January); low birth weight, preschool age, male gender, child care attendance, siblings.[23] When data from cohorts having predominantly term infants was analysed, an increased RSV infection as well as other negative outcomes were seen in low birth weight infants.[24-26]

Clinical profile showed that respiratory distress (20/20), cough (100%), fever (85%), cold (75%), nasal discharge (75%) were most common symptoms. [Table 1] Almost same findings were seen in a study done by Vahini V, *et al.* in which cough was seen in all the patients (75/75), followed by dyspnea (96%) and fever (80%).[27] In Ganavi *et al.* study, all the children had cough and in a study done by Soleimani *et al.* 89% babies had cough, with fever in 72% and dyspnoea was observed in 71% of children.[27,28] 25% of children had apnoea and cyanosis in our study whereas Soleimani *et al.* observed apnea in 14% of children.[28,29] Sahleh *et al.* found more than half of his patients were having chest wall retractions and in our study also subcostal (83%) and intercostal (70%) retractions were seen in more than half patients.[15] Ganavi *et al.* found tachypnea and chest indrawing in 100% of children whereas in our study tachypnoea was seen in 75% of children.[28] 18/20 patients required assisted ventilation and 3/20 (15%) patients were mechanically ventilated in our study whereas in a study done by Sahleh's *et al.* 38.6% required mechanical ventilation and all patients were given assisted ventilation either via nasal cannula or mask.[15] In a study by Gokce *et al.* and Soleimani *et al.* wheezing was present in 58% and 79% of children in contrast to our study in which 80% the children presented with wheeze. [Table 1] Crepititions were seen in 15/20 (75%) patients which is similar to findings in a study from Doha in which 73.5% patients had crepts.[29-31]

In our study, we noticed that a higher CRP and procalcitonin was observed in most of the patients median value being 27.335 and 13.92, respectively, unlike the study done in Serbia in which CRP was less.[4,32] An elevated CRP levels points towards bacterial causes and is a nonspecific marker for viral infection. In patients with raised CRP, antibiotic was also given, thus, 13 out of 20 patients were prescribed antibiotics. Since, patients showing high CRP levels have a high probability of bacterial coinfection, this correlation would help the clinician to decide the treatment of patients in which antimicrobial therapy is necessary. Ioannis *et al.* have emphasised the need for a deeper analysis of patient data for newly evolved drugs or agents against RSV thus leading to personalised treatment regimens.[33] This requires a combined diagnostic, clinical and research efforts which is time of need for advancing paediatric care so as to improve clinical outcomes and limit global RSV morbidity and mortality.[33]

Studies have shown that hepatitis is commonly seen in association with bronchiolitis in patients of RSV with a prevalence of 49% in ventilated children, and the disease takes a grave course if transaminases levels are elevated.[34,35] More than 80% of children were observed with increased AST and ALT levels. Similar observation was made by Jeon *et al.* who observed that, 19.4% of patients with lower respiratory tract viral infection had hepatic dysfunction, the frequency of hepatic damage being highest in RSV positive patients (50%).[36]

Majority of RSV infected patients present to the primary health care physician in out-patient department. This was also seen by Thomas *et al.* also who reported that 93% of young symptomatic RSV patients were managed on outpatient basis which supports the fact that the first person who comes in contact with an RSV infected child is a primary health care physician.[14] Thus, this study helps us to understand the RSV disease burden as well as associated premorbid conditions affecting the disease severity.

Acknowledgement

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Summary

1. It has been recognised as one of the most important reasons for hospitalisation of children of all age group (particularly <5 years) presenting with acute LRTI.
2. Seasonal trends of RSV are associated with increase in incidence.
3. The study emphasises on the role of primary and secondary health care givers to make an early diagnosis as per the symptomatology to aid in infection control and diagnosis.
4. Majority of RSV infected patients present to the primary health care physician in out-patient department, thus there is a need to strengthen the hospital facilities and improve patient care.
5. This study has helped us to understand the RSV disease burden as well as associated premorbid conditions affecting the disease severity.

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Conflicts of interest

There are no conflicts of interest.

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