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Research Article

Influence of some viral agents on the severity of acute bronchiolitis in infants

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Summary

Acute bronchiolitis is the most common lower respiratory tract disease in infancy and the leading cause of hospitalization in children under two years of age. Many authors emphasize the importance of viral agents for the clinical course of the disease. This study aimed to assess the clinical severity of acute bronchiolitis in hospitalized infants. We examined 49 hospitalized children between 1 month and 2 years with acute bronchiolitis. The study investigated viral aetiology and markers of inflammatory activity. Disease severity was assessed according to the ReSVinet scale. A viral agent was identified in 59.2% of cases, with RSV (respiratory syncytial virus) as the predominant aetiology in 32.7%, followed by rhinovirus in 14.0%, human metapneumovirus and Bocavirus in 4.1% each, and Adenovirus, Influenza type A, and Parainfluenza virus in 1 (2.0%) each. No causative agent was identified in 40.8% of cases. We observed a mild clinical course in 30.6%, mostly with combined viral infection; a moderate course in 61.2%, mainly with RSV aetiology; and a severe course in 8.2%, in which no predominant etiological factor was identified. Further investigations are needed to clarify the relationship between viral aetiology and disease severity.

Key words: Acute bronchiolitis, ReSVinet scale, viral infection

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Introduction

Acute bronchiolitis is one of the most common causes of infant admission to intensive care units (Choi and Lee 2012). As an acute lower respiratory tract infection, bronchiolitis in infancy is caused by various viruses (Nagakumar and Doull 2012). A significant proportion of infants experience at least one episode in their first year of life, and 2–3% require hospitalization (Petrarca et al. 2017). Bronchiolitis in infants has a high morbidity but low mortality due to continuous improvements in pediatric intensive care. It typically begins with fever and rhinorrhea, gradually developing signs such as cough, wheezing, and tachypnoea, forced exhalation, worsening of general condition, cyanosis, chest retractions, and the use of accessory muscles as signs of respiratory failure (Oymar et al. 2014). Respiratory syncytial virus (RSV) is widely recognized as the most common cause of bronchiolitis in infants. Other implicated viruses

include adenovirus, influenza virus, parainfluenza virus, rhinovirus, human coronavirus, and metapneumovirus (Biagi et al. 2020). Viral co-infections are found in approximately 30% of hospitalized infants. The infectious process affects the small bronchi and bronchioles and, together with increased mucus secretion and bronchial smooth muscle constriction, is a prerequisite for the development of broncho-obstructive syndrome and respiratory failure (Bosis et al. 2008).

Aim

This study aimed to evaluate the influence of different respiratory viruses, including RSV, human rhinovirus (HRV), human metapneumovirus (hMPV), influenza virus (IV), parainfluenza viruses (PIV), and adenoviruses (AV), on the clinical severity of acute bronchiolitis in infants.

Materials and methods

The study was designed as a prospective investigation. It was conducted over 6 months (September 2022 to February 2023). It included 49 children (mean age of 12.5 ± 11.9 months) diagnosed with acute bronchiolitis at the Department of Pediatrics, Dr. George Stranski University Hospital - Pleven.

Children aged 1–24 months presenting with clinical signs of an infectious syndrome, bronchial obstruction, varying degrees of respiratory failure, and radiological findings consistent with acute bronchiolitis were eligible for inclusion. Patients with chronic pulmonary or cardiac disorders, including bronchopulmonary dysplasia, cystic fibrosis, primary ciliary dyskinesia, congenital heart defects, or other non-infectious causes of obstructive airway disease, were excluded from the study.

A universally validated scoring system is not available, and we used the ReSVinet Scale, a reference scale for assessing clinical severity in children under 2 years of age with acute respiratory disease, primarily used in acute bronchiolitis. The ReSVinet Scale evaluates seven criteria – general condition, fever, nutrition, medical intervention, apnea, difficulty breathing, and respiratory rate. Each of them is scored from 0 to 3, except for fever, which is scored from 0 to 2. The total value is obtained by summing all components, each with a score of 0–20. Severity is commonly stratified into mild (0–6 points), moderate (7–13 points), and severe (14–20 points) categories (Justicia-Grande and Martinón-Torres 2019).

The viral nucleic acids were automatically extracted using the Sa Mag Viral Nucleic Acid Extraction kit (Sacace). Screening of respiratory specimens for respiratory syncytial virus (RSV), human metapneumovirus (HMPV), parainfluenza viruses (PIV), rhinoviruses (RV), adenoviruses (AdV), and bocaviruses (BoV) was performed using single-plex real-time PCR assays and an AgPath-ID One-Step RT-PCR kit (Applied Biosystems, Thermo Fisher Scientific. Primers, probes, and thermocycling conditions used in the study were identical to those previously described (Kodani et al. 2011).

Ethical approval was granted by the Ethics Committee of the Medical University – Pleven (Approval No. 694, May 31, 2022). Written informed consent for participation in the study was obtained from the parents or legal guardians of all enrolled patients.

Statistical methods

Descriptive statistics for qualitative variables were presented as frequencies and percentages, while quantitative variables with normal distributions were summarized using means and standard deviations. Quantitative variables with skewed distributions were reported using medians and interquartile ranges. We used non-normally distributed quantitative variables and box plot diagrams for visual representation.

The distributional characteristics of continuous variables were assessed with the Shapiro–Wilk test. Since several variables deviated from normality, non-parametric statistical methods were considered appropriate. Comparisons of continuous clinical and laboratory parameters across the three predefined severity groups (mild, moderate, severe) were performed with the Kruskal–Wallis H test. To determine whether there was a statistically significant difference between two independent groups, the Mann-Whitney U test was used. The relationship between the ReSVinet score and co-infection status was analyzed using point-biserial correlation. A two-tailed significance level of $p < 0.05$ was applied for all statistical tests.

All analyses were performed using IBM SPSS Statistics v.25 and Microsoft Excel 2019.

Results

All participants underwent ResVinet Score testing. The distribution of scores showed that 25 (51.0%) had 9 or fewer points; 6 (12.2%) scored 10 points; 10 (20.4%) scored 11; 3 (6.1%) scored 12; 1 (2.0%) scored 13; 3 (6.1%) scored 14; and 1 (2.0%) scored 15 points. No child scored higher than 15.

Based on the ReSVinet scale, the examined children were classified into three groups. The first group included 15 (30.6%) patients with MILD, the second group included 30 (61.2%) patients with MODERATE, and the third group included 4 (8.2%) patients with SEVERE respiratory distress. The erythrocyte sedimentation rate (ESR) in the examined children ranged from 3 to 47 mm/h. Seventeen patients (34.7%) required oxygen supplementation. Nineteen children (38.8%) (mostly from the mild group) were discharged within 5 days, while those with moderate or severe disease remained hospitalized for 6–11 days. Mean laboratory values were as follows: mild group – CRP 1.2 mg/L; WBC 8.5 × 10^9/L; ESR 19 mm/h; moderate group – CRP 1.7 mg/L; WBC 13.2 × 10^9/L; ESR 21 mm/h; severe group – CRP 12.3 mg/L; WBC 15.7 × 10^9/L; ESR 26 mm/h. A statistically significant difference in WBC was found across the three groups ($H = 10.215$, $df = 2$, $p = 0.006$) (Table 1).

Table 1. Laboratory parameters.

Clinical indicators	Respiratory distress							
	Mild		Moderate		Severe		Total	
	Me	Min–Max	Me	Min–Max	Me	Min–Max	Me	Min–Max
CRP	1.2	0.2–9.4	1.7	0.1–46.4	12.3	1.2–122.2	1.7	0.1–122.2
WBC	8.5	2.3–22.7	13.2	7.3–30.0	15.7	10.4–17.7	11.7	2.3–30.0
ESR	19.0	3.0–47.0	21.0	9.0–32.0	26.0	22.0–29.0	21.0	3.0–47.0

Virologic analysis identified a single viral pathogen in 29 infants (59.2%). RSV was found in 16 patients (32.7%). RSV co-infection was found in 6 patients (12.2%), rhinovirus in 8 children (14.0%), metapneumovirus in 2 children (4.1%), Bocavirus in 2 children (4.1%), and Adenovirus, Influenza type A, and Parainfluenza virus in 1 (2.0%) each. No viral agent was detected in 20 infants (40.8%).

A statistically significant negative correlation was observed between the ReSVinet score and the presence of viral co-infection (rpb = −0.434, N = 28, p = 0.021), indicating a moderate effect size. Because the distribution of ReSVinet scores did not meet the assumptions of normality (Shapiro–Wilk = 0.904, df = 38, p = 0.003), non-parametric methods were used. A Mann–Whitney U-test confirmed a significant difference between the groups (U = 35.500, z = −2.315, p = 0.021).

The infants without a detected virus had a median ReSVinet score of 10.5 (IQR = 4.25), while those with monoinfection had a slightly higher median of 11.0 (IQR = 1.75). The lowest clinical severity was observed in infants with co-infection, who had a median score of 6.0 (IQR 4.50).

These findings suggest that monoinfection is associated with both higher severity scores and greater variability compared to co-infection or the absence of detectable viral pathogens (Fig. 1).

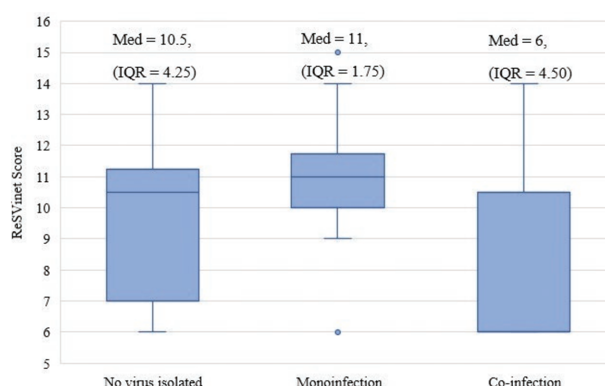

Figure 1. ReSVinet Score in monoinfection and co-infection.

Based on the virology analysis, among infants with a mild course of acute bronchiolitis (n = 15), RSV was identified in 3 patients (6.1%), co-infection was observed in 5 infants (10.2%), and 7 children (14.3%) had no viruses detected. In the group with moderate disease severity (n = 30), RSV was detected in 12 patients (24.5%), RV in 2 infants (4.1%), HMPV in 1 patient (2.0%), and influenza type A in 1 patient (2.0%). In contrast, 12 children (24.5%) had a negative etiological analysis. In the severe disease group (n = 4), three infants tested positive for viruses, with RSV, RSV+RV, and RV identified, respectively, whereas one child (2.0%) had no viruses detected.

Discussion

Most studies show that acute bronchiolitis occurs in 60–85% of infants up to 12 months of age (Jartti et al. 2009; Mikalsen et al. 2012). Almost every child becomes infected with RSV by the age of 2 years, with peak incidence between 2 and 3 months (Leung et al. 2005). Multiple studies have shown that RSV is the most common virus in infants with acute bronchiolitis. In 2019, Korsun et al.

reported RSV as the most frequently detected etiological agent of bronchiolitis, followed by Rhinovirus and HMPV (Korsun et al. 2019). In the 49 children we examined, RSV was the most common virus, isolated from 33% of infants with acute bronchiolitis. The study found that after RSV, the second most common virus in infants with acute bronchiolitis was rhinovirus (16%), followed by metapneumovirus (4%), Bocaviruses (4%), Influenza type A (2%), and Parainfluenza virus (2%). A similar study found rhinovirus (RV) to be the second most common virus (14–30%) in infants with acute bronchiolitis, followed by RSV. Next in prevalence are human bocavirus, human metapneumovirus, enteroviruses, adenoviruses, coronaviruses, and influenza viruses (Presti et al. 2024). The present study concluded that RSV was the most common cause of acute bronchiolitis in the infants studied, and it caused longer hospital stay and longer course of oxygen therapy. Using molecular diagnostic tests, various studies have found that children with acute bronchiolitis have a high frequency of viral co-infection (in 15–40% of children), with RSV and rhinovirus being the most common (Barr et al. 2019). Several authors have reported that children with RSV-hMPV co-infection are at increased risk of admission to the intensive care unit, with a noted tendency toward longer hospital stays in this subgroup. The same analyses found no significant differences in the clinical course of RSV and hMPV mono-infections when considered separately (Semple et al. 2005; Li et al. 2020; Althouse et al. 2021).

Conversely, other studies provide evidence to the contrary, indicating that co-infection with hMPV and RSV does not result in a more severe disease course than single-virus infections (Wilkesmann et al. 2006; Miller et al. 2013). A recent study showed that viral co-infection did not increase the likelihood of PICU admission compared with monoinfection. However, the length of hospital stay (LOS) was longer in children with viral co-infection than in those infected by a single pathogen (Bermúdez-Barrezueta et al. 2023). The causes of acute bronchiolitis in infants vary by season and latitude. It has not been definitively established whether a specific viral induction determines disease severity, although most studies report severe disease in the presence of RSV infection (Ramagopal et al. 2016).

Reasons for divergent severity outcomes between viral monoinfection and viral co-infection may include modulation of the host immune response, including viral interference phenomena, differences in host susceptibility, the pathogenic characteristics of specific viral combinations, and methodological factors related to study design and analysis. Variations in age distribution, socioeconomic status, viral circulation patterns, climate, and seasonality, as well as environmental exposures such as household crowding, tobacco smoke, and air pollution, can significantly influence both the incidence and clinical presentation of acute bronchiolitis.

Fares M. et al. report that WBC count alone was not a significant predictor of bacterial co-infection in children hospitalized with bronchiolitis (Fares et al. 2011). C-reactive protein (CRP), white blood cell count (WBC), and erythrocyte sedimentation rate (ESR) are commonly used inflammatory markers that help distinguish viral from bacterial involvement in acute bronchiolitis. In predominantly viral infections, these markers are usually low to moderately elevated, reflecting a milder systemic inflammatory response. Marked increases in CRP, WBC, and ESR, however, are more suggestive of bacterial co-infection and have

been reported in children with RSV bronchiolitis and bacterial involvement. Higher values of these indicators may also correlate with more severe clinical presentation, supporting their use as accessible tools for assessing disease severity and guiding clinical decisions (Begum et al. 2024).

Lastly, the primary limitation of this study is the relatively small sample size, particularly within the group of infants with severe disease. This constraint is largely attributable to the study being conducted as part of a research project with limited financial resources, which markedly limits the robustness and interpretability of statistical comparisons across severity categories and increases the risk of unstable estimates.

Conclusion

RSV was the most commonly identified etiological agent in infants with acute bronchiolitis and was associated with longer hospital stay and more severe clinical manifestations. However, other respiratory viruses, including rhinovirus, human metapneumovirus, bocavirus, adenovirus, and influenza, also contributed significantly to disease burden and may lead to diverse clinical outcomes.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: Medical University Pleven.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

No use of AI was reported.

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Author contributions

Conceptualization: MP. Data curation: MP. Formal analysis: MP, NKB. Funding acquisition: MP. Investigation: PVD, MP, AR. Methodology: EMD, AR. Project administration: MP, PVD. Supervision: NKB. Validation: EMD, AR, NKB, PVD. Visualization: EMD. Writing – original draft: MP. Writing – review and editing: NKB, EMD.

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Data availability

All of the data that support the findings of this study are available in the main text.

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