

Main Causes of Viral Bronchiolitis in Babies – Systematic Review

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ABSTRACT

Introduction: Acute bronchiolitis is almost exclusively caused by viral infection in children under 2 years of age. It is a secondary inflammatory viral infection of the lower airways, causing obstruction of the lower respiratory tract.

Objective: Review the literature to verify the main causes of viral bronchiolitis in babies.

Methods: This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (Simple Multi-Attribute Rating Technique using Exploiting Rankings).

Results: A comprehensive systematic search of the literature yielded a total of 439 articles referring to the main causes of bronchiolitis in infants. Of these, 29 articles were eligible to be included in this systematic review.

Conclusion: The study concluded that bronchiolitis research has seen a significant increase in research and publications, but further investigation is needed to improve our understanding and management of this condition.

KEYWORDS: Bronchiolitis; Causes; Babies.

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INTRODUCTION

Acute bronchiolitis is almost exclusively caused by viral infection in children under 2 years of age. It is a secondary inflammatory viral infection of the lower airways, causing obstruction of the lower respiratory tract (GÓMEZ-ACEBO et al., 2021; SILVER; NAZIF, 2019). Its symptoms almost always begin with rhinitis, which can progress to respiratory difficulty progressing to wheezing, tachypnea and the use of accessory muscles (SILVER; NAZIF, 2019). It is important that the doctor is able to make the differential diagnosis of bronchiolitis and other respiratory diseases, such as early-onset asthma or aerodigestive conditions (LINSSEN; SCHECHTER; RUBIN, 2023).

The most common cause of bronchiolitis is respiratory syncytial virus (RSV), accompanied by other viruses such as influenza, rhinovirus or metapneumovirus. Premature babies, with congenital heart disease (CHD), with bronchopulmonary dysplasia (BPD) have a high risk of having severe bronchiolitis, leading to hospitalization during the epidemic season (FAUROUX et al., 2020).

More than 30 million lower respiratory tract infections occur due to RSV infection in children under 5 years of age, 3.2 million of which require hospitalization and there are an average of 200,000 deaths per year (DALZIEL et al., 2022; FUJIOGI et al., 2019; NIEVAS - SORIANO et al., 2023). Infections caused by RSV lead to 45 to 54% of babies under 6 months of age being hospitalized (NIEVAS - SORIANO et al., 2023).

This pathology, in addition to being a major public health problem, also generates social alarm when in periods of high incidence (between November and April, with an increase in cases in January and February) (EFSTATHIOU et al., 2020) they lead parents to loss of working days, as their children often end up needing isolation and home care and even hospital admissions (BILLARD; BONT, 2023; DÍEZ-GANDÍA et al., 2021; NIEVAS - SORIANO et al., 2023; PICHE - RENAUD et al., 2021).

In this context, the objective of this study was to systematically review the literature to verify the main causes of viral bronchiolitis in babies.

METHODS

This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*). The work carried out is of a qualitative and quantitative nature. Qualitative data analysis was carried out intuitively and inductively during the survey of the theoretical framework. It

is also quantitative through the use of the multi-criteria method. In addition, there is also a numerical experimental study in order to simulate an article selection situation based on the observed criteria.

Based on bibliographical research, they were located in the following databases: *US National Library of Medicine* (PubMed), Web of Science; Science Direct (Elsevier); Wiley; SpringerLink; Taylor and Francis and EBSCO. In addition, searches were carried out using bibliographic references of studies that relevantly addressed the topic on the *Google Scholar search platform* (Google, USA).

The search in the databases was carried out using the terminologies registered in the Health Sciences Descriptors created by the Virtual Health Library developed from the *Medical Subject Headings of the US National Library of Medicine*, which allows the use of common terminology in Portuguese, English and Spanish. The present study sought to investigate the literature on the main causes of bronchiolitis in babies. To this end, the descriptors “Bronchiolitis; Causes and Babies”, initially in English, and additionally in Spanish and Portuguese.

As a tool to support decision-making in the selection and prioritization of articles, a set of criteria were considered essential to represent the state of the art of the topic under study. This method has the following characteristics: (i) rigorous logic allows the method to be accepted as a decision support tool; (ii) simple to understand and apply with easy-to-interpret results.

References from selected works were also searched for other documents of potential interest. Once qualified for full-text review, articles were included in the qualitative review if they met the following inclusion criteria: a) contained data on bronchiolitis; b) causes; c) babies. Articles were excluded if they were reports, banners or conference abstracts. There was no review of confidential health information and the study was non-interventional. Therefore, ethics committee approval was not necessary. In the end, the result obtained totaled 29 articles that covered the desired characteristics for the study.

RESULTS

A comprehensive systematic search of the literature yielded a total of 439 articles referring to the main causes of bronchiolitis in infants. From this, the SMARTER method (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*) was chosen. Of these studies, 90 articles were suitable for full-text screening and 52 articles were included for data extraction. Of these, 15 studies were excluded due to data overlap. Here, 29 articles were included for systematic review. In Figure 1, we describe the strategy for selecting articles on the topic in question.

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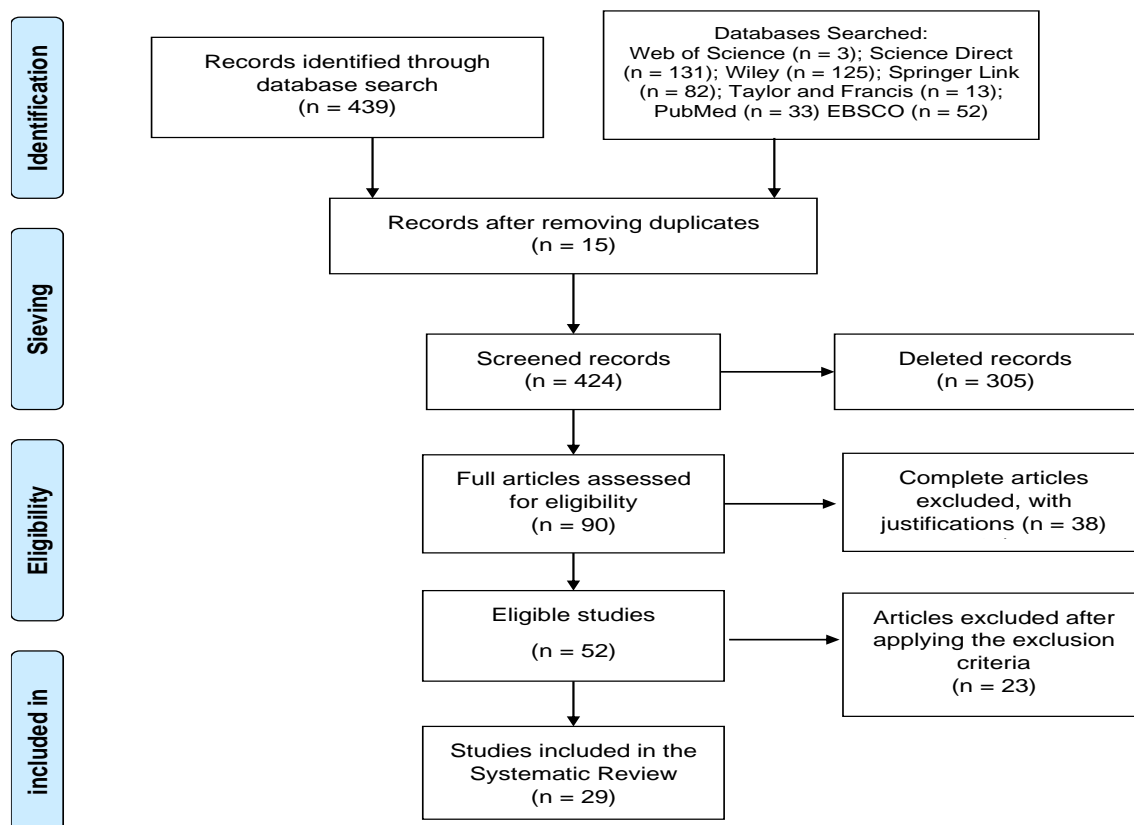


Figure 1. Article search strategy

Most frequent causes:

Respiratory syncytial virus (RSV)

RSV is a non-segmented RNA virus that belongs to the *Pneumovirus genus of the Paramyxoviridae* family and is the main cause of acute viral bronchiolitis in children (SUH et al., 2022; YAO et al., 2021).

As it is a very contagious respiratory virus, it can cause mild to severe illnesses in children. Contamination with this virus causes cough, runny nose and fever (SONI; KABRA; LODHA, 2023).

It is estimated that this virus infects more than 60% of all children during the first year of life, infects almost all children by the age of 2 and that severe infection is associated with an increased risk of recurrent wheezing in childhood. Inefficient antiviral immune responses are considered to be related to acute and long-term changes in airway functions (MANTI et al., 2023; ROSSI et al., 2022).

Adenovirus

Human adenoviruses (HAdVs) are members of the Adenoviridae family and are responsible for approximately 5 to 18% of bronchiolitis in babies, which is normally sporadic and is similar to other diseases associated with other viral agents (LU; ZHENG, 2018; SHIEH, 2022).

Bronchiolitis caused by Adenovirus can occasionally progress to pneumonia, which can also be fatal or lead to chronic diseases and serious residual lung damage (SHIEH, 2022).

It can be followed by serious sequelae, such as bronchiolitis obliterans, leading to damage to the lower respiratory tract. This may occur after a severe respiratory infection in previously healthy preschool children. HAdV infection may be one of the main causes of bronchiolitis obliterans in childhood (SHIEH, 2022; ZHONG; LIN; DAI, 2020).

Influenza virus

The influenza virus has a great transmission potential and causes acute infection in the respiratory system. There are four types of influenza, A, B, C and D, with A and B being largely responsible for the biggest pandemics. In children under 2 years of age, when infected by this virus, they present a high risk of hospitalization, and in children under 6 months of age there is a high mortality rate (FLERLAGE et al., 2021; SAÚDE, 2023).

This virus was associated with 13% of acute respiratory infections in childhood, and represented around 2 to 10% of all deaths from these infections, with 99% of these deaths occurring in developing countries (WANG et al., 2020)

Enterovirus

These viruses are responsible for many diseases, such as: myocarditis, neurological diseases, febrile illnesses, encephalitis, aseptic meningitis and paralysis. Species C and D are mainly found in the respiratory tract, causing upper and lower respiratory symptoms. Since the first isolation in 1962 of enterovirus D68, it has been almost exclusively associated

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with respiratory diseases. It has characteristics shared with rhinoviruses that are from the *enterovirus* genus, within the *Picornaviridae* family (GONZÁLEZ-SANZ et al., 2019).

Rhinovirus

The rhinovirus is very contagious and ubiquitous, belonging to the *Picornaviridae* family. It is normally transmitted through direct exposure to respiratory droplets and/or micro droplets, although this transmission can also occur through contaminated surfaces, including direct contact between people (BIAGI et al., 2020).

Rhinovirus, together with respiratory syncytial virus, are the most common pathogens associated with bronchiolitis and represent the main cause of hospitalization in infants. They are common in infections and co-infections along with other viruses, and their impact has been the subject of studies by several researchers and presented controversial results. Some studies demonstrate that there is no influence on the clinical course, while others demonstrate that virus infections result in more serious clinical conditions and a greater risk of complications. Around 20–40% of children with bronchiolitis are found to be infected with rhinovirus (BIAGI et al., 2020).

DISCUSSION

In recent years throughout the world, there has been a considerable increase in care for children with bronchiolitis, as an increase in admissions to intensive care has been noted. Infections caused by RSV in children under 5 years of age have been causing an annual global impact, being reported and predicted in 33 million children (range: 21.6–50.3 million), of these, 3.2 million hospitalizations (range: 2.7–3.8 million) and 120,000 deaths (range: 94,000–149,000) (LINSSEN et al., 2022; MAHANT et al., 2022; MANTI et al., 2023).

A cohort study carried out by Fauroux et al. (2020), demonstrated that among infants, 6.0% were premature and 2.0% had ≥ 1 chronic condition, including 0.2% bronchopulmonary dysplasia (BPD) and 0.2% hemodynamically significant congenital heart disease. Bronchiolitis hospitalization rates varied between seasons (min: 1.26% in 2010–2011; max: 1.48% in 2012–2013; $p < 0.001$). Except for omphalocele, the following conditions were associated with an increased risk of hospitalization for bronchiolitis: solid organ (9.052; 95% CI, 4.664–17.567) and stem cell transplants (6.012; 95% CI, 3.441–10.503), dystrophy muscle (4.002; 95% CI, 3.1095–5.152), cardiomyopathy (3.407; 95% CI, 2.613–4.442), HS-CHD (3.404; 95% CI, 3.153–3.675), congenital lung disease and/or anomalies bronchial disorders, Down syndrome, tracheoesophageal fistula, diaphragmatic hernia and pulmonary hypertension.

Another cohort study carried out in Spain, with around a thousand newborns, demonstrated that breastfeeding was associated with a lower risk of bronchiolitis and fewer episodes of bronchiolitis. Early cessation of breastfeeding

before the second or fourth month of life was associated with the risk of bronchiolitis and the number of bronchiolitis episodes. The results also demonstrated that the duration of breastfeeding, regardless of the exclusivity of breastfeeding (breastfeeding and mixed breastfeeding) from 0 to 6 months, is a crucial factor in reducing the incidence of bronchiolitis and the number of episodes of bronchiolitis in the first year of life (GÓMEZ-ACEBO et al., 2021).

Suh et al. (2022), demonstrated in their study that from 2009 to 2019, acute bronchiolitis due to RSV was the leading primary diagnosis for all Medicaid and private insurance hospitalizations in the United States. For those who are insured by Medicaid, acute bronchiolitis due to RSV accounted for 10.0% of total pediatric hospitalizations from January 2009 to September 2015 and 9.8% from October 2015 to December 2019. For private insurance, represented 9.2% and 8.9% of total child hospitalizations in the 2 time periods, respectively (SUH et al., 2022).

The study carried out by Zhong; Lin; Dai (2020), concluded that children who have a longer-lasting fever, dyspnea or require mechanical ventilation in the acute phase are highly likely to develop obliterative bronchiolitis, making early diagnosis and good clinical monitoring necessary.

In relation to the influenza virus, the study carried out by Wang et al. (2020), demonstrated that meta-estimates of the incidence of acute lower respiratory infections increase with the patient's age (p for linear trend < 0.05). The rate of hospital admission for influenza virus-associated acute lower respiratory infections was lower in neonates (0.9 per 1,000 neonates per year, 95% CI 0.4–1.8) and was consistently higher in infants older than 1 month (1.6–1.9 per 1000 children per year) in developing countries.

The study carried out by Jartti et al. (2020), on the role of the virus in asthma, demonstrated that it remains to be clarified whether bronchiolitis contributes to the development of asthma or is a marker of susceptibility to asthma. In this sense, rhinovirus may be a revealing factor for those with early airway inflammation, low interferon responses demonstrating impaired viral defense, and/or genetic variations that serve as markers of asthma risk.

In research carried out in a tertiary hospital in Germany, it was shown that enterovirus D68 was associated with severe obstructive bronchitis and pneumonia. These diseases are recognized by higher rates in oxygen use. Furthermore, premature babies also had higher rates of oxygen demand (BAERTL et al., 2021).

Although bronchiolitis is a very common disease in childhood, agreement on various diagnostic and treatment characteristics of this pathology has not yet been reached, demonstrating that professionals must continue their searches so that unnecessary tests and treatments are not used on these patients (CARLONE et al., 2023).

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FINAL CONSIDERATIONS

Despite improvements through vaccination programs, childhood acute respiratory infections still contribute to a significant burden of disease and are a leading cause of death. The baby's immature immune response means this age group is susceptible to a variety of viral, bacterial and fungal respiratory infections.

The results of this study suggest that bronchiolitis is a topic of significant interest and concern for researchers and healthcare professionals. Bronchiolitis research has seen a significant increase in research and publications, but further investigation is needed to improve our understanding and management of this condition.

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