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REVIEW ARTICLE

Epidemiological and genetic characteristics associated with the severity of acute viral bronchiolitis by respiratory syncytial virus☆

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KEYWORDS
Bronchiolitis;
Risk factors;
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Abstract
Objective: to assess the epidemiological and genetic factors associated with severity of acute viral bronchiolitis (AVB) by respiratory syncytial virus (RSV).
Data source: the key words ''bronchiolitis'', ''risk factor'', ''genetics'' and ''respiratory syncytial virus'', and all combinations among them were used to perform a search in the PubMed, SciELO, and Lilacs databases, of articles published after the year 2000 that included individuals younger than 2 years of age.
Data synthesis: a total of 1,259 articles were found, and their respective summaries were read. Of these, 81 were selected, which assessed risk factors for the severity of AVB, and were read in full; the 60 most relevant studies were included. The epidemiologic factors associated with AVB severity by RSV were prematurity, passive smoking, young age, lack of breastfeeding, chronic lung disease, congenital heart disease, male gender, ethnicity, viral coinfection, low weight at admission, maternal smoking during pregnancy, atopic dermatitis, mechanical ventilation in the neonatal period, maternal history of atopy and/or asthma during pregnancy, season of birth, low socioeconomic status, Down syndrome, environmental pollution, living at an altitude > 2,500 meters above sea level, and cesarean section birth. Conversely, some children with severe AVB did not present any of these risk factors. In this regard, recent studies have verified the influence of genetic factors on the severity of AVB by RSV. Polymorphisms of the *TLRs*, *RANTES*, *JUN*, *IFNA5*, *NOS2*, *CX3CR1*, *ILs*, and *VDR* genes have been shown to be associated with more severe evolution of AVB by RSV.

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Conclusion: the severity of AVB by RSV is a phenomenon that depends on the varying degrees of interaction among epidemiological, environmental, and genetic variables.

PALAVRAS-CHAVE
Bronquiolite;
Fatores de risco;
Vírus sincicial respiratório;
Genética

Características epidemiológicas e genéticas associadas à gravidade da bronquiolite viral aguda pelo vírus sincicial respiratório

Resumo

Objetivo: avaliar os fatores epidemiológicos e genéticos associados à gravidade da Bronquiolite Viral Aguda (BVA) pelo Vírus Sincicial Respiratório (VSR).

Fonte dos dados: foram utilizados descritores *''bronchiolitis''*, *''risk factor''*, *''genetics''* e *''respiratory syncytial virus''* e todas as combinações entre eles, nas bases de dados PubMed, SciELO e Lilacs publicados após o ano de 2000 e que incluíram indivíduos menores de dois anos de idade.

Síntese dos dados: foram encontrados 1.259 artigos e lidos seus respectivos resumos. Destes foram selecionados 81 que avaliaram fatores de risco para a gravidade da BVA para leitura na íntegra, e foram incluídos os 60 estudos mais relevantes. Os fatores epidemiológicos associados com a gravidade da BVA pelo VSR foram: prematuridade, tabagismo passivo, baixa idade, ausência de aleitamento materno, doença pulmonar crônica, cardiopatia congênita, sexo masculino, etnia, coinfecção viral, baixo peso na admissão hospitalar, tabagismo materno na gestação, dermatite atópica, ventilação mecânica no período neonatal, antecedente materno de atopia e/ou asma na gestação, estação do nascimento, baixo nível socioeconômico, síndrome de Down, poluição ambiental, morar em altitude acima de 2.500 metros do nível do mar e parto cesariana. Em contrapartida, algumas crianças com BVA grave não apresentam nenhum desses fatores de risco. Neste sentido, estudos recentes têm verificado a influência de fatores genéticos relacionados à gravidade da BVA pelo VSR. Polimorfismos dos genes *TLRs*, *RANTES*, *JUN*, *IFNA5*, *NOS2*, *CX3CR1*, *ILs* e *VDR* têm-se mostrado associados com a evolução mais grave da BVA pelo VSR.

Conclusão: a gravidade da BVA pelo VSR é um fenômeno dependente da interação entre variáveis epidemiológicas, ambientais e genéticas em seus diferentes graus de interação.

Introduction

Acute viral bronchiolitis (AVB) caused by respiratory syncytial virus (RSV) is the primary infection of the lower airways in children under 2 years of age worldwide, and it is the main cause of hospitalization in this age group in developed countries.[1] Although all children are infected with RSV by the age of three, most infections are mild and have no sequelae. The mechanisms involved with the severity of AVB caused by RSV are not yet fully understood. Why does RSV infection present such variable evolution in different patients? Why does one child with RSV remain asymptomatic and another child dies? When assessing the severity of AVB caused by RSV, which factors are more often associated: genetic and/or epidemiological/environmental factors? These questions have intrigued researchers and remain without definitive answers.

There are 3,000 to 4,000 deaths annually in the United States due to AVB caused by RSV.[2] The prevalence of hospitalization due to RSV in the United States is 48.9 per 1,000 in children younger than 3 months, 26 per 1,000 in those younger than 1 year, and 1.8 per 1,000 in children aged 1 to 5 years, with 132,000 to 172,000 hospitalizations/year due to RSV in children under 5 years.[3] In the United States, there are, on average, 22.8 visits to the emergency room caused by RSV per 1,000 infants; 29% of whom are hospitalized. That represents an annual spending of 50.5 million dollars on emergency room visits and 650 million dollars on hospitalizations.[4] In other regions, the rate of hospitalization per 1,000 infants with RSV varies from 8.7 in Australia[5] to 60 in Japan.[6] In Australia, the incidence of RSV is from 110.0 to 226.5 per 1,000 infants, and the annual cost is estimated at $ 50 million dollars, which is more significant than the costs of *Influenza* and *Rotavirus* infections.[5] In Europe, RSV is responsible for 45% of hospitalizations for lower respiratory infection in children younger than 2 years.[6]

In Brazil, a study of 5,304 children younger than 1 year showed that 113 (2.1%) were hospitalized due to AVB.[7] Among the children hospitalized for RSV, 2.7% were admitted to the intensive care unit (ICU), 1.5% required assisted ventilation, and 0.2% died.[8]

Infection by RSV has variable severity with clinical manifestations from mild symptoms in the upper respiratory tract to bronchiolitis and pneumonia, and may develop into the severe form, requiring ICU admission and mechanical ventilation, and at times leading to death. To date, the treatment of AVB by RSV is supportive. It has been demonstrated that, in the United States, of 1.1 million children younger than two years hospitalized for RSV in a period of eight years, the highest percentage of hospitalizations occurred between 3