

Risk Factors for RSV Hospitalization in Healthy Preterm Infants

A Meta-analysis

To the Editors:

Respiratory syncytial virus (RSV) infection is an important cause of childhood morbidity from acute lower respiratory tract infections worldwide. In a previous publication in this journal,¹ we presented a systematic review and qualitative synthesis of risk factors for RSV hospitalization and incidence and short- and long-term outcomes of RSV hospitalization for otherwise healthy preterm infants born at 29 to 35 weeks gestation age (WGA). One conclusion from that study was that the strength of evidence for the studied outcomes was strong only for risk factors for an RSV hospitalization for otherwise healthy preterm infants of 32/33 to 35 WGA. In this letter, we add to that information the results of a quantitative assessment of the risk of RSV hospitalization in these preterm infants.

We used RevMan software (Version 5.3, The Nordic Cochrane Centre, Copenhagen) to estimate the pooled random-effects and fixed-effects treatment estimates using the inverse-variance method and, more specifically, Mantel-Haenszel fixed effect method, and the DerSimonian and Laird method for random effects.² We evaluated heterogeneity by comparing study designs through visual inspection of forest plots, the I^2 statistic, and the χ^2 Cochrane Q heterogeneity test. Primary analyses included all studies with available data. We included 4 cohort studies and 1 case-control study.¹

All authors are employees of RTI International; none has a financial interest in the sales of palivizumab, which is manufactured by AstraZeneca/Medimmune who provided an unrestricted grant to RTI International to perform the review and meta-analysis. AstraZeneca/Medimmune had no role in the development of the protocol, performance of the literature searches, abstraction of the data or preparation of the meta-analysis. The other authors have no conflicts of interest to disclose. Address for correspondence: Josephine Mauskopf, PhD; E-mail: jmauskopf@rti.org.

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TABLE 1. Meta-Analysis Results

Risk Factor	Random-effects Model		Fixed-effects Model	
	Odd Ratio (95% Confidence Interval)	<i>P</i>	Odd Ratio (95% Confidence Interval)	<i>P</i>
Siblings	2.36 (1.92–2.91)	<0.00001	2.35 (1.92–2.88)	<0.00001
Young_age	3.30 (2.62–4.17)	<0.00001	3.27 (2.67–4.00)	<0.00001
Atopy	1.25 (0.57–2.71)	0.58	1.53 (1.11–2.11)	0.01

Review of the evidence revealed 3 risk factors amenable to pooling: (1) presence of school-age siblings (herein, “siblings”); (2) born close to start of RSV season or early in the season (herein, “young_age”) and (3) family history of atopy (“herein atopy”).

Meta-analysis of the available quantitative evidence identified from the systematic literature review indicated that the presence of siblings and born close to the start of or early in the RSV season are significant risk factors for RSV infection requiring hospitalization (see Table 1). No relationship between family history of atopy and RSV hospitalization could be established.

Our meta-analyses had some limitations. The first is the small size of the evidence base for our target population, in terms of numbers of included studies and risk factors amenable to pooling. In addition, all data were drawn from observational studies, which are more likely than randomized controlled trials to exhibit systematic bias and imbalanced comparison groups. All study estimates were covariate-adjusted, but there was no adjustment for unknown or unreported confounding factors.

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Acute Cerebellitis in a Child With Scrub Typhus

To the Editors:

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi*. It is transmitted by bite of the larval forms (chiggers) of Trombiculidae mite; hence it is also known as chigger borne typhus.¹ Scrub typhus has varied central nervous system manifestations.² Although aseptic meningitis is reported in 10%–25% of the cases, isolated cerebellar involvement in children with scrub typhus is rare.³ Here, we describe a 9-year-old boy with acute onset cerebellar ataxia as a manifestation of scrub typhus.

A 9-year-old boy living in the foothills of Himalayas presented with acute onset fever, headache, vomiting and swaying to the left side. There was no history suggestive of seizures, focal deficit, rash, recent immunization, animal or insect bite. On examination, he was febrile, had conjunctival suffusion and icterus. There was no eschar. Neurologic examination revealed horizontal gaze nystagmus and left-sided truncal ataxia. The rest of the systemic examination was normal.

Laboratory investigations revealed leukocytosis (12.2×10^9 cells/L) with predominance of lymphocytes (88%) and with neutropenia (10%) and thrombocytopenia (76×10^9 cells/L). Liver function tests showed elevated transaminase values (aspartate transaminase, 2504 IU/L; alanine transaminase, 1573 IU/L), conjugated hyperbilirubinemia (3.8 mg/dL) and coagulopathy. Lumbar cerebrospinal fluid showed no cells, normal glucose (94 mg/dL) and protein (56 mg/dL). Gram stain was negative, and the culture was sterile. Cerebrospinal fluid polymerase chain reaction for herpes simplex virus DNA was negative. Investigations

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