

**Prevalence, immunopathogenesis and antioxidant status of children
with Acute Respiratory Infections due to Respiratory Syncytial Virus
and Human Metapneumovirus and risk factors for disease severity in
Yemen**

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Abstract

Aims: to establish the prevalence of RSV and HMPV in Yemeni children with ARI, describe the risk factors for disease severity, the cytokine (IL6, TNF- α , IL7, IL10, IL12 and INF- γ) and chemokine (IL8 and RANTES) concentrations in children with RSV and/or HMPV and their association with disease severity. To determine serum micronutrients and C- reactive protein concentrations in children with RSV and/or HMPV with mild and severe ARI.

Methodology: Children < 2 years old with signs and symptoms of ARI attending a reference hospital in Sana'a, Yemen, were enrolled during 2002 and 2003. RSV and HMPV were identified using RT-PCR. Children with mild/moderate ($pO_2 \geq 88\%$) hypoxia were compared to those with severe hypoxia ($pO_2 < 88\%$). Cytokines and chemokines were measured by ELISA. Inductive Coupled Plasma Mass Spectrometry was used to measure zinc, selenium and copper and a High Performance Liquid Chromatography to measure serum vitamins A and E concentrations.

Results: RSV was identified in 40%, HMPV in 7% and RSV/HMPV co-infections in 4% of the children. Group A was the predominating RSV. The period with high RSV and HMPV incidence occurred from December to March but both viruses were detected throughout the study. Single RSV and HMPV infections were undistinguishable clinically and dual infections were common. The factors independently associated with an increased risk of severe hypoxia due to RSV were age ≤ 3 months, the child not having his/her vaccines up to date, the presence of a smoker at home and using a cooking fuel other than gas. In contrast, only age ≤ 3 months, having a history of recurrent ARI and using a source of fuel other than gas were the only risk factors found to be independently associated with an increased risk of severe HMPV. RSV and HMPV infections in infants differ significantly in regard to the type of induced immune response elicited and coinfections modified the production of cytokines. Young age modifies immune responses against the infections. There was an inverse association of IL7 with hypoxia due to RSV. Micronutrients deficiency is widespread in our study population (especially with RSV) and was associated with disease severity and inflammatory stress with an inverse relationship between zinc and copper concentrations and zinc/copper ratios of children with RSV and HMPV.

Conclusion: RSV and HMPV are important causes for ARI in Yemen. This thesis describes the immunological mechanisms observed in RSV and HMPV infections and the risk factors associated with disease severity. This information can be used to inform the development of curative and preventive strategies for acute respiratory infections and for the monitoring of curative interventions. Micronutrient deficiencies are highly prevalent in children with ARI and micronutrient supplementation may decrease the risk for developing severe RSV and HMPV disease.