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Title: Host and viral factors predicting severity of rhinovirus-associated wheeze

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Body: Background Rhinovirus (RV) is a common cause of wheeze in childhood. Personal history of atopy, presence of siblings and day care attendance are known risk factors for severe RV-associated wheezing but objective markers predicting disease severity are lacking. We aimed at identifying such markers in a cohort of preschool children hospitalized for RV-associated wheezing. Methods Direct immunofluorescence for RV and other viruses was performed on nasopharyngeal aspirates (NPA) within the first 24 hours of hospitalisation of children aged 0-6 years. RV load, interferons (γ and λs) and cytokines (IL-4, 6, 8, 13, IP-10) were quantified by RT-PCR and ELISA and related to clinical parameters. Results Within a 4-years period (2007- 2011), we included 126 children (median (range) age: 1.66 (0.40-5.81) years). Presence of RV was confirmed by RT-PCR in all NPA samples. RV load was inversely related to age (r=-0.22, p=0.02) and correlated with the pro-inflammatory cytokines IL-8 (r=0.23, p=0.01) and IL-6 (r=0.35, p=0.001). There was no relationship between RV load or any IFNs cytokine level and clinical outcome parameters (clinical severity scores, length of hospitalisation and duration of oxygen therapy). Post-hoc analysis revealed a trend towards higher IL-6 levels of children with prolonged oxygen need (>1 vs. ≤1 days): (135 (5-789) vs.16 (5-244) pg/ml, p=0.07). Conclusions In our cohort, RV load and related antiviral and pro-inflammatory responses were not associated with disease severity. This may be due to the wide age-range of subjects studied. Whether IL-6 levels in NPA may help to predict clinical outcome in subgroups of children with RV-associated wheezing illnesses needs to be evaluated in further studies.