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Respiratory infections in Eñepa Amerindians are related to malnutrition and *Streptococcus pneumoniae* carriage

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Summary *Objectives:* High acute respiratory tract infection (ARTI) rates are observed in indigenous populations. We assessed the role of viral infections and nasopharyngeal bacterial carriage in ARTIs in Eñepa Amerindians from Venezuela.
Methods: In 40 children aged 0–10 years with ARTIs, healthy nearest-age sibling controls and their mothers the presence of *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*/*psittachi* and 15 respiratory viruses was investigated.
Results: *S. pneumoniae* was the most frequently detected pathogen, with carriage rates of 75% and 38% in children and mothers respectively. In children, *S. pneumoniae* carriage was associated with ARTI risk in multivariate analysis (OR 14.1, 95% CI 1.4–137.7). Viral infections were not associated with ARTI risk. *S. pneumoniae* carriage was common in children of all ages while viral co-infections were more frequently present in children under 4 years compared to older children (46% vs. 17%, $p < 0.01$). An increase of one unit height-for-age Z score (i.e. improved chronic nutritional status) was associated with decreased odds of *S. pneumoniae* colonization in multivariate analysis (OR 0.66, 95% CI 0.44–0.99).

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Conclusions: In Eñepa children high *S. pneumoniae* carriage rates associated with a poor nutritional status contribute to the development of ARTIs.

Introduction

Acute respiratory tract infections (ARTIs) are among the leading causes of childhood mortality worldwide, responsible for about two million child deaths annually.[1] Pneumonia rates are especially high in low-income countries and underlying malnutrition is a major risk factor for pneumonia in children from developing countries.[2] Recent estimates suggest that *Streptococcus pneumoniae* and *Haemophilus influenzae* together account for more than 50% of childhood pneumonia deaths each year.[3,4] Acquisition of nasopharyngeal carriage of these bacteria is an initial step in the process leading to invasive bacterial diseases.[5] The increased ability to simultaneously test for multiple pathogens has highlighted the potential role of co-colonization with multiple respiratory tract bacteria and co-infection with viral infections in progression to disease after colonization.[6–9]

In indigenous children ARTIs, in particular acute lower respiratory tract infections (ALRTIs), are more common and associated with higher morbidity than among non-indigenous age-matched counterparts in the same region. In a population-based birth cohort study performed in Australia, pneumonia rates in Aboriginal children were 13.5 times higher than in non-Aboriginal children (95% CI 12.8–14.4).[10] In the United States, The ALRTI-associated hospitalization rate was 3-fold higher for American Indian/Alaska Native children than for the general U.S. population in retrospective analyses.[11,12] The high prevalence rates of ARTIs, including ALRTIs and acute otitis media (AOM), in Australian and North American native children have been associated with increased carriage of viral and bacterial respiratory tract pathogens compared to non-natives.[13–18] While in Australia, Canada and the U.S. native populations make up only two to four percent of the population, ten percent of the South American population consists of indigenous people.[19–21] There is a lack of health research reports concerning the principal clinical presentations and infectious etiologies of ARTIs in indigenous people from the South American region.[19]

The Eñepa (or Panare) Amerindians inhabit the Cedeño Municipality of the Venezuelan state of Bolívar, characterized by a forest-savanna landscape. They live in around 40 isolated communities where they have very little interaction with other indigenous or non-indigenous Venezuelan populations. Pneumococcal vaccinations have not been introduced in this population. We investigated bacterial nasopharyngeal carriage, viral infections and nutritional status in Eñepa Amerindian children aged 0–10 years with and without ARTIs and their mothers.

Patients and methods

Study population and sampling

In August 2011, during the rainy season, five geographically isolated Eñepa communities (Biscochuelo, Colorado, El Guamal, Macanilla, Quebrada seca) were visited for primary health care services. During these visits, all inhabitants were registered. Of the 145 children aged 0–10 years present in the 5 communities at the time of survey, 40 (28%) were diagnosed with an ARTI, including AOM. Nasopharyngeal samples were taken of these children and of 40 nearest-age full sibling controls aged 0–10 years and within 5 years of patient age. When several siblings fulfilled these eligibility criteria, the sibling whose age was nearest to that of the case was included. When no siblings fulfilled these criteria ($n = 3$), the nearest-age cousin living in the same household was included as a matched control. Nasopharyngeal samples were also taken of mothers of the included children ($n = 43$). As nasopharyngeal samples alone may be insufficient to detect colonization by *S. pneumoniae* and *H. influenzae*,[22] oropharyngeal swabs for bacterial isolation were taken as well. Nasopharyngeal samples for bacterial and viral isolation were obtained with a flexible swab (Copan Italia). Oropharyngeal samples were obtained by use of rigid cotton-tipped applicators. Swabs were transported at 4°C–7°C within 4 h after sampling, in STGG medium[23] for bacterial isolation and in TE (10 mM Tris–HCl, 1 mM EDTA, pH 8) for virus isolation, to a −20 °C freezer. Within 7 days, swabs were transferred to −70 °C where they were stored until microbiological and virological analyses. Physical examinations, including ear examination by pneumatic otoscopy and anthropometric measurements of children and mothers, were performed and documented on a standardized data collection sheet.

Study definitions

ARTIs were classified as upper respiratory tract infection (URTI) or ALRTI. A diagnosis of URTI was made when at least 2 common cold symptoms (fever, rhinorrhea, sore throat, headache, cough, muscle aches) with at least 1 symptom involving the respiratory tract (rhinorrhea, sore throat, cough) in the absence of an increased respiratory rate, chest indrawing, or auscultatory findings such as crepitations or rhonchi, were present.

ALRTIs were classified as follows:

- Pneumonia: the presence of (1) a history of cough or difficulty in breathing and (2) chest indrawing or increased respiratory rate ($\geq$60 breaths/min for children $<$2 months of age, $\geq$50 breaths/min for children 2–11 months of age,