

Association between Pathogen Load in the Upper Respiratory Tract and Severe Acute Respiratory Infections in Guatemalan Adults: *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*

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Introduction

- The causal attribution of bacterial pathogens to severe acute respiratory infections (SARI) is challenging because many bacteria are frequently detected in the upper respiratory tract of asymptomatic persons.
- Estimating the exposure-response relationship between pathogen load and probability of disease may help distinguish harmless colonizers from causes of clinically significant disease as well as improve accuracy of attributable fraction estimates for some etiologies

Methods

- Study Design:** case-control study
- Study Period:** October 2013 — October 2015
- Exposure:** PCR Cycle threshold values (proxy for pathogen load)
- Cases:** adults with SARI (acute onset of respiratory infection with history of fever or measured fever $\geq 38^{\circ}\text{C}$ and cough, with onset within the last 7 days, requiring hospitalization)
- Controls:** adults without symptoms of respiratory infection in the prior week, enrolled from trauma and orthopedic inpatient wards
- Procedures:** Nasopharyngeal and oropharyngeal specimens were collected from all participants and tested for pathogens using rRT-PCR.
- Statistical Analysis:** The Wilcoxon rank sum test was used to compare the distributions and median Ct values between adults with SARI and asymptomatic adults in whom *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae* were detected.

Purpose

To determine whether bacterial load, as measured by real-time PCR (rRT-PCR) cycle threshold (Ct) values, differs between asymptomatic adults and adults with severe acute respiratory infections.

Results

Table. Frequency of select bacterial pathogen detections among adults with SARI and among asymptomatic adults, Guatemala, 2013-2015

Bacteria	SARI, n (%) (n = 304)	Asymptomatic, n (%) (n = 174)
<i>H. influenzae</i> –all types	60 (19.7)	49 (28.2)
<i>K. pneumoniae</i>	17 (5.6)	18 (10.3)
<i>M. catarrhalis</i>	38 (12.5)	19 (10.9)
<i>S. aureus</i>	36 (11.8)	24 (13.8)
<i>S. pneumoniae</i>	75 (24.7)	45 (25.9)

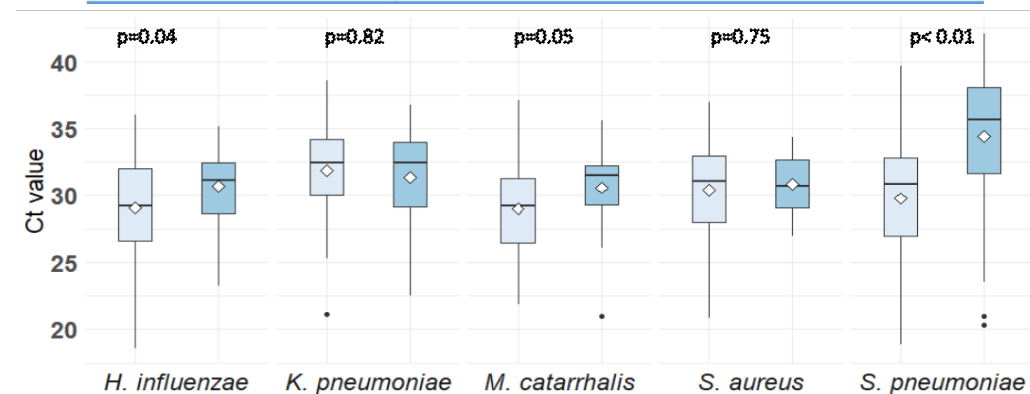


Figure. Distributions of Ct values among adults with SARI (light blue) and asymptomatic adults (dark blue) in whom a given bacterial pathogen was detected. Lower Ct values indicate higher bacterial load. Horizontal lines through boxes indicate group medians and diamonds indicate group means.

Results

- M. catarrhalis*, *S. aureus*, and *S. pneumoniae* were detected with similar frequency in adults with SARI and in asymptomatic adults, whereas *H. influenzae* and *K. pneumoniae* were detected more frequently in asymptomatic adults.
- The greatest difference in Ct value distributions between ill (median Ct=30.8) and asymptomatic adults (median Ct=35.6) was found in *S. pneumoniae* detections ($p < 0.01$)

Conclusions

- Ct values may provide insight into the etiologic role *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* in SARI, despite the similar frequency of detection of these bacteria among both ill and asymptomatic adults.
- Future work will normalize Ct values to account for variation in testing and analysis and explore the use of Ct values to estimate population attributable fractions of respiratory infections.

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