Symptomatic Infants have Higher Nasopharyngeal SARS-CoV-2 Viral Loads but Less Severe Disease than Older Children.

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Dear editor:

Published data suggest lower rates of severe coronavirus disease 2019 (COVID-19) in pediatric age groups [1,2]. However, the relative contribution of infants and children to community transmission is not known. Data from China suggest that children were infected early in the outbreak [3]. A report published in this journal described the presence of a high nasopharyngeal (NP) viral load of severe acute respiratory coronavirus 2 (SARS-CoV-2) in a well infant [4]. Whether this observation is generalizable to symptomatic infants, and how it compares to NP viral loads in older children and adolescents is not known. Studies in adults have demonstrated a positive correlation between viral load and COVID-19 severity [5]. While some data have suggested a higher disease severity in infants [2,6], how NP viral load correlates with severity across the pediatric age spectrum has not been firmly established.

Here we report NP viral load among infants, children and adolescents who were hospitalized and discharged from our children's hospital from March 14th to April 24th, 2020. All patients were tested either in the emergency department or during inpatient hospitalization based on symptoms suggestive of COVID-19. For each patient, we extracted age, time from reported symptom onset to the date of test, and severity of disease during hospitalization. Severity of COVID-19 disease was determined by: i) the need for respiratory support with non-invasive positive pressure ventilation and/or mechanical ventilation or, ii) ICU admission.

All testing was performed by reverse transcriptase polymerase chain reaction with the cobas SARS-CoV-2 assay (Roche Molecular Systems, Inc., Branchburg, NJ). Cycle threshold (Ct) values, which are inversely proportional to viral RNA concentration, were

used to measure relative viral loads. Target 2, a conserved region of the structural protein envelope E-gene, was used for these purposes as it was the most consistently amplified target. We used Student's t-tests to compare mean Ct values between age groups and Fisher's exact tests to compare categorical variables.

Among 57 patients testing positive for SARS-CoV-2, 20 (35.1%) were infants 12 months of age or younger. Older children and adolescents ranged from 1 year to 21 years of age. Mean NP viral load was significantly higher in infants as compared to older children and adolescents (mean Ct 21.05 vs 27.25, $p<0.01$) (**Figure 1)**. However, a significantly lower proportion of infants had severe disease as compared to the older patients (N = 1 (5%) vs. N = 12 (32.4%), p=0.02). Mean time to test positivity from symptom onset was lower in infants than older children (2 vs. 3.8 days, $p<0.01$). Similar proportions in both groups were tested within seven days of symptom onset (91.2% vs. 100%, p=0.47).

Our report suggests symptomatic infants have higher NP viral loads at presentation but develop less severe disease as compared to older children and adolescents. Whether this is attributable to slightly earlier presentation to clinical care vs. host biology requires investigation. These data have implications for mitigating spread, especially in congregate settings (e.g. child care centers) or hospital units (e.g. neonatal intensive care units) that serve this group.

Funding: none

Financial Disclosures: There are no financial disclosures to report on any of the authors

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Figure 1. Nasopharyngeal swab viral loads and severity of disease compared across Infants vs. Older children