

Title: Neonatal Pulmonary Function Tests and Clinical Respiratory Outcomes at 1 Year of Age in Infants Born to COVID-19 Positive Mothers

Authors: Katy L. Ruch, MD, Kseniya Parkhotyuk, RRT, Diane Schilling, RRT, Kristin Milner, MS and Cindy T McEvoy, MD, MCR

Institution: Oregon Health & Science University

Background: 2019 Coronavirus disease (COVID-19) preferentially affects adults often with bilateral pneumonia and respiratory failure. Data for potential vertical transmission of the virus from the mother to fetus is evolving, but there is emerging evidence for increased rates of pregnancy related complications in mothers found to be COVID-19 positive during pregnancy. There is currently no data on how being exposed to COVID-19 in utero may impact fetal lung growth and development.

Methods: We performed a prospective cohort study of neonates born to COVID-19 positive mothers identified through an ongoing registry at Oregon Health & Science University, to provide early quantification of pulmonary function tests (PFTs) in infants born to COVID-19 positive mothers. We then compared the infant's PFTs to matched healthy term and preterm reference infants. The comparison group was obtained from a previous reference/control group from our PFT laboratory. It was comprised of infants without clinical respiratory disease (<12 hours of >0.21 fraction of inspired oxygen) which were matched to the study infants for gestational age, birth weight, sex, race, and postmenstrual age (PMA) at the time of the PFT. Respiratory compliance (Crs) and resistance (Rrs), were measured with the single breath occlusion technique and flow volume loop characteristics were also analyzed. Additionally, through chart review and standardized respiratory questionnaires (RQ), we assessed the frequency of reactive airway and allergic symptoms such as cough, wheeze, rhinitis and eczema in these patients.

Results: Nine infants (range of 28 to 38.4 weeks gestation) born to COVID-19 positive mothers were studied and compared to 9 matched infants. The median interval between the maternal positive COVID test and delivery was 8 days. At delivery, four of the pregnant women had symptoms including fever, shortness of breath, and cough with 2 requiring respiratory support. Five of the infants were admitted to the NICU due to prematurity and as per protocol, 3 had COVID-19 PCR testing which was negative. The remainder of the infants remained on the Mother Baby Unit and were discharged at a median of 2 days of life. The PFTs of the infants born to the COVID-19 positive mothers were comparable to the results of the matched infants and within normal range for these measurements in our PFT laboratory (Table 1). Upon follow up at 1 year of age via medical chart review and via a standardized RQ, 33% of study infants born to mothers diagnosed with COVID-19 at delivery or during gestation, had reported episodes of wheeze, 1 of which required treatment. Of the reference infants, 44% reported episodes of wheeze, but none required treatment. Recurrent cough (when not otherwise ill) was reported in 22% of study infants and 11% of reference infants. Of all study infants 67% reported either reactive airway or allergic symptoms in the first year of life.

Conclusion: This early report describes the PFTs in infants born to COVID-19 positive mothers and presents PFT results of matched healthy reference infants. Although preliminary, the PFT and clinical respiratory outcomes at 1 year of age appear comparable between groups, but an expanded study population and longer term follow-up is needed and is ongoing.

Table 1. Characteristics & Pulmonary Function of Studied Infants

	Study Infants (COVID-19 positive mothers) (n=9)	Reference Infants (n=9)
Birth weight (g)*	2567 (2088, 3478)	2577 (2054, 3330)
Gestational age (wks)*	35.0 (33.0, 37.0)	34.6 (33.2, 37.1)
Male / female	6/3	6/3
Race: White (%)	100%	100%
Hispanic/Non Hispanic	6/3	6/3
Tidal volume/kg**	6.8 ±1.1	6.6 ±1.2
PMA at PFT**	36.2 ±1.4	35.3 ±2.2
Crs (mL/cmH ₂ O/kg)**	1.21 ±0.32	1.24 ±0.24
Rrs (cmH ₂ O/mL/sec)**	0.058 ±0.014	0.046 ±0.013

*Median (25th and 75th percentile); ** Mean ± SD. P = NS for Clinical Characteristics and PFTs between groups.

Table 2. Respiratory Outcomes at ~1 Year Postnatal Age

	Study Infants	Reference Infants
Mean PNA at RQ	11.5 mo.	14.3 mo.
Total reporting wheeze	3 (33%)	4 (44%)
Medication for wheeze*	1 (11%)	0
Recurrent cough**	2 (22%)	1 (11%)
Mean # of colds	2.67 ±4.4 (Median 2)	2.1 ±2.5 (Median 2)

*Albuterol, **without other clinical illness