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Vertical transmission of SARS-CoV-2: consider the denominator

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Objective

More than 82,000 pregnant women in the United States have tested positive for SARS-CoV-2.¹ Published estimates of the incidence of vertical transmission—the passage of SARS-CoV-2 from mother to baby during pregnancy or childbirth—range from 1-3%, but these reports

may be limited in their methodology.²⁻⁴ The largest systematic review and meta-analysis to date reports a pooled estimate of 3.2%,² yet includes data from cohort studies and case series published early in the pandemic, when reports on outcomes of SARS-CoV-2 positive newborns were urgently needed to guide clinical management and potentially overrepresented. Here we provide additional data on vertical transmission from a multi-center cohort of pregnant women with SARS-CoV-2 infection.

Study Design

Women with a positive nasopharyngeal PCR for SARS-CoV-2 during pregnancy who delivered from March 22 through December 20, 2020 at one of three hospitals in Boston, MA—Massachusetts General Hospital (MGH), Brigham and Women's Hospital (BWH), and Beth Israel Deaconess Medical Center (BIDMC)—were included. These hospitals perform approximately 15,000 deliveries per year, accounting for approximately 75% of annual deliveries in Boston. The Mass General Brigham and BIDMC Institutional Review Boards approved this study. Some of the participants included in this report of vertical transmission have been included in prior reports describing different outcomes.

Inpatient universal testing protocols for SARS-CoV-2 were in place since early April (MGH/BWH) or May (BIDMC). Outpatient testing was performed by clinical indication, i.e. a known exposure or symptoms. Consistent with the American Academy of Pediatrics (AAP) guidelines released April 2, 2020,⁵ neonatal testing by nasopharyngeal PCR was performed at 24 hours of life only in newborns of mothers with SARS-CoV-2 who were considered infectious at the time of delivery and at 48 hours or later at the discretion of the provider or Infection Control.

Results

There were zero cases of SARS-CoV-2 infection identified in 369 newborns born to 354 women who tested positive for SARS-CoV-2 in pregnancy. Of the 369 delivered newborns, 159 newborns (43%) were tested at least once for SARS-CoV-2 during the delivery hospitalization, with 149 newborns (94%) receiving a test at 24 hours of life. Of the 354 women infected with SARS-CoV-2 during pregnancy included in this cohort, 140 (40%) delivered within 14 days of diagnosis. The median interval from maternal diagnosis of SARS-CoV-2 infection to delivery was 29 days [IQR 2-108]. Asymptomatic or mild disease was noted in 259 women (73%).

Table 1 depicts maternal and neonatal characteristics.

Conclusion

We identified no cases of vertical transmission in our cohort, which includes a large proportion of women with asymptomatic or mild disease. Newborns were tested in accordance with hospital infection control policies (e.g. not tested if born to convalescent mothers). While vertical transmission does occur, data from our centers suggest the incidence of SARS-CoV-2 vertical transmission, as detected by neonatal nasopharyngeal swab, is likely lower than the 1-3% estimated in previous reports.²⁻⁴

The challenge in selecting the denominator for calculating the incidence of vertical transmission is illustrated by the CDC report on 2,869 newborns of women with SARS-CoV-2 infection during pregnancy.⁴ Test results were available on 610 newborns—only 21% of the cohort—of which 16 (2.6%) tested positive. More than 60% of newborns without testing information were delivered greater than 10 days from maternal infection. These newborns were either not tested or had a negative result which, unlike a positive result, is not mandated to be

reported to the state. If all newborns born to women with SARS-CoV-2 infection in pregnancy were included in the denominator, the incidence of identified vertical transmission would be 0.6% (16 of 2,869), not 2.6%.

Consensus on how to define, detect, and report vertical transmission of SARS-CoV-2 is lacking. Although both the AAP and CDC recommend testing all infants born to mothers with active SARS-CoV-2 infection at the time of delivery, the optimal strategy for evaluating vertical transmission in the setting of early (first and second trimester) pregnancy infections is not known. Although nasopharyngeal PCR-based testing of infants born to convalescent women is likely to be low yield, sampling the fetal compartment during maternal SARS-CoV-2 infection to assess for transmission could incur risk without clear benefit. Estimates of the incidence of vertical transmission that exclude untested newborns should be interpreted with caution, as untested newborns cannot demonstrate their presumed SARS-CoV-2 negative status. We assert that the appropriate denominator to estimate the incidence of vertical transmission includes all newborns of women infected with SARS-CoV-2 during pregnancy.

Abbreviations:

MGH, Massachusetts General Hospital; BWH, Brigham and Women's Hospital; BIDMC, Beth Israel Deaconess Medical Center; PCR, polymerase chain reaction; AAP, American Academy of Pediatrics; IQR, interquartile range; CDC, Centers for Disease Control and Prevention

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Table 1. Characteristics of pregnant women testing positive for SARS-CoV-2 and frequency of newborn SARS-CoV-2 testing

	All (n=354)	MGH (n=144)	BWH (n=130)	BIDMC (n=80)
Maternal disease severity ^a , n (%)				
<i>Asymptomatic</i>	66 (19)	31 (22)	22 (17)	13 (16)
<i>Mild</i>	192 (54)	76 (53)	75 (58)	41 (51)
<i>Moderate</i>	59 (17)	22 (15)	23 (18)	14 (18)
<i>Severe</i>	25 (7)	11 (8)	7 (5)	7 (8)
<i>Critical</i>	12 (3)	4 (3)	3 (2)	5 (6)
GA at diagnosis in completed weeks, median [IQR]	32 [22-38]	32 [23-38]	33 [23-37]	32 [19-36]
GA at diagnosis by trimester, n (%)				
<i>First</i>	37 (10)	12 (8)	16 (12)	9 (11)
<i>Second</i>	92 (26)	38 (26)	29 (22)	25 (31)
<i>Third</i>	225 (64)	94 (65)	85 (65)	46 (58)
GA at delivery in completed weeks, median [IQR]	39 [37-39]	39 [38-39]	39 [37-39]	38 [37-39]
Mode of delivery, n (%)				
<i>Vaginal delivery</i>	221 (62)	89 (62)	83 (64)	49 (61)
<i>Cesarean section</i>	133 (38)	55 (38)	47 (36)	31 (39)
Preterm birth (<37 weeks) ^b , n (%)	53 (15)	18 (13)	18 (14)	17 (21)
Days from first positive test to delivery, median [IQR]	29 [2-108]	33 [2-101]	27 [2-106]	26 [3-113]
Women delivering <14 days from date of diagnosis, n (%)	140 (40)	56 (39)	49 (38)	33 (41)
Total newborns, n	369	150	135	84
<i>Positive for SARS-CoV-2^c, n (%)</i>	0 (0)	0 (0)	0 (0)	0 (0)
<i>Negative for SARS-CoV-2^c, n (%)</i>	159 (43)	69 (46)	60 (44)	30 (36)
<i>Not tested for SARS-CoV-2^c, n (%)</i>	210 (57)	81 (54)	75 (56)	54 (64)
Incidence of vertical transmission, % [95% CI] ^d	0 [0-1.0]	0 [0-2.4]	0 [0-2.7]	0 [0-4.3]
Newborns tested for SARS-CoV-2 ^c after birth, n	159	69	60	30
<i>Tested at 24h only</i>	105 (66)	49 (71)	38 (63)	18 (60)
<i>Tested at 24h and 48h-72h</i>	31 (20)	15 (22)	4 (7)	12 (40)
<i>Tested at 24h and 4d-14d</i>	13 (8)	4 (6)	9 (15)	0 (0)
<i>Tested at other timepoints</i>	10 (6)	1 (1)	9 (15)	0 (0)

MGH, Massachusetts General Hospital; BWH, Brigham and Women's Hospital; BIDMC, Beth Israel Deaconess Medical Center; GA, gestational age; IQR, interquartile range.

^aDefined by the National Institute of Health and endorsed by the Society for Maternal-Fetal Medicine

^bIncludes both iatrogenic and spontaneous preterm birth

^cBy clinically available nasopharyngeal PCR for SARS-CoV-2

^dNumber of newborns testing positive for SARS-CoV-2 divided by number of newborns delivered to SARS-CoV-2 positive women (n=369 all hospitals, n=150 MGH, n=135 BWH, n=84 BIDMC). 95% CI calculated by exact (Clopper-Pearson) method.