

5.1.2e  
 #COVID19Series  
 Are Pregnant Women More Likely to Acquire SARS-CoV-2?

### #COVID19Series

## Are Pregnant Women More Likely to Acquire SARS-CoV-2?

- Most overall population studies **do not provide pregnancy status** for females.
- While initial data from CDC did not suggest higher prevalence in pregnant women (CDC COVID-19 Response Team. MMWR. 2020 Mar 31), some more recent data is of concern.
- In a study of universal pre-procedural SARS-CoV-2 rPCR tests before all surgeries or deliveries in 5,543 persons in St. Louis hospital May-July 2020, positivity rates were higher in Ob than Surgical unit patients (Kelly JC et al. Am J Obstet Gynecol. 2020 Sep 21:S0002-9378(20)31102-9).

|                  | Ob Unit (N=922) | Surgical Unit (N=5,011) | Adjusted* OR   |
|------------------|-----------------|-------------------------|----------------|
| Aax SARS-CoV-2 + | 25 (4.7%)       | 14 (0.3%)               | 4.7 (2.3-10.6) |

\*Adjusted for age, race

- CDC recently reported 9% of reproductive-aged women (8,207/91,412) with lab-proven SARS-CoV-2 between Jan-June were pregnant; this was higher than expected, as CDC estimates ~5% of women aged 15-44 years are pregnant at a given point in time (Ellington S et al. MMWR 2020 Jun;69:769-75).

5.1.2e

### #COVID19Series

## Prevalence of SARS-CoV-2 Infection in Pregnant Women, by Sampling Strategy

Allotey J et al. BMJ. 2020 Sep 1;370:m3320

- Systematic review; prevalence of positive SARS-CoV-2 rPCR in 26 studies including 11,432 pregnant women attending or admitted to hospital

| Study               | n      | Prevalence (%) | 95% CI |
|---------------------|--------|----------------|--------|
| Overall             | 11,432 | 10             | 7-13   |
| Universal screening | 1,000  | 7              | 4-10   |
| Symptom-based       | 10,432 | 18             | 10-28  |

- Overall 10% prevalence SARS-CoV-2 infection in pregnant women hospitalized in pandemic locales
- Infection prevalence rates >15% were all from US, except 1 study from France.
- Universal screening: rPCR of all pregnant women presenting at labor/delivery. Prevalence 7% (95% CI 4-10%)
- Symptom-based: rPCR only if symptoms of infection or history of close contact to individual with infection. Prevalence 18% (95% CI 10-28%)

5.1.2e

### #COVID19Series

#### Do Symptoms Differ in Pregnant vs Non-Pregnant Women with COVID-19?

Ellington S et al. MMWR. 2020 Jun;69:769-75

- CDC compared COVID-19 disease among 8,207 pregnant and 83,205 non-pregnant women of reproductive age in US with positive SARS-CoV-2 rtPCR reported January 22-June 7 2020.

| Symptom             | Pregnant (%) | Non-Pregnant (%) |
|---------------------|--------------|------------------|
| Cough               | 50%          | 50%              |
| Fever               | 34%          | 42%              |
| Myalgia             | 21%          | 28%              |
| Chills              | 20%          | 28%              |
| Headache            | 21%          | 28%              |
| Dyspnea             | 30%          | 30%              |
| Sore throat         | 27%          | 31%              |
| Diarrhea            | 14%          | 23%              |
| N/V                 | 20%          | 16%              |
| Ab. Pain            | 10%          | 12%              |
| Runny nose          | 9%           | 10%              |
| Loss of taste/smell | 17%          | 17%              |

- Symptomatic pregnant and nonpregnant women with COVID-19 reported similar frequencies cough (>50%) and dyspnea (30%), but pregnant women less frequently reported fever, muscle aches, chills, headache and diarrhea.

5.1.2e

### #COVID19Series

#### Universal Screening for SARS-CoV-2: Majority of Infected Pregnant Women Are Asymptomatic

| Author        | Country           | Total n | % rPCR       | % Asymptomatic |
|---------------|-------------------|---------|--------------|----------------|
| Waldman       | US (NY)           | 274     | 15.4% (n=33) | 73.3% (n=29)   |
| Waldman       | US (NY)           | 161     | 19.2% (n=31) | 65.6% (n=21)   |
| Chen et al    | US (CT)           | 778     | 3.9% (n=31)  | 73.3% (n=22)   |
| Costello      | US (Boston)       | 757     | 2.6% (n=20)  | 42% (n=9)      |
| Lubchenco     | US (Seattle)      | 389     | 2.7% (n=5)   | 20% (n=1)      |
| Buckley       | US (NY)           | 160     | 17.5% (n=29) | 100% (n=5)     |
| Blitz         | US (NY)           | 325     | 17.5% (n=57) | 100% (n=5)     |
| Fernandez     | NY (Albany)       | 1559    | 3.1% (n=49)  | 79.2% (n=49)   |
| Shah          | US (Chicago)      | 630     | 3.1% (n=20)  | 55.1% (n=27)   |
| Bennett et al | US (CA)           | 492     | 3.6% (n=23)  | 43.5% (n=19)   |
| Falkner et al | US (CA)           | 2623    | 2.0% (n=53)  | 70% (n=7)      |
| Wu et al      | UK (London)       | 100     | 0.8% (n=7)   | 100% (n=7)     |
| Chen et al    | Portugal (Lisbon) | 103     | 7.0% (n=9)   | 88.9% (n=8)    |
| Chen et al    | Japan (Tokyo)     | 52      | 11.7% (n=6)  | 91.8% (n=11)   |
| Chen et al    | China (Guangdong) | 52      | 3.8% (n=2)   | 100% (n=2)     |
| Chen et al    | China (Guangdong) | 545     | 0.4% (n=2)   | 45% (n=6)      |

- 15 papers reporting on universal nasopharyngeal SARS-CoV-2 rPCR testing of 10,108 women presenting in labor in hospitals in midst of COVID-19 pandemic
- 348 (3.4%) were positive on SARS-CoV-2 rPCR.

5.1.2e

5.1.2e

#COVID19Series

### Risk Factors for Hospitalization with COVID-19 in Pregnancy

The UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group (UKOSS). *BMJ* 2020 Jun 8;369:m2107

- Population-based surveillance system, including all 194 maternity units in the UK.
- Between March 1 – April 14, 2020, 86,293 pregnant women admitted to maternity units; 427 (5%) had confirmed SARS-CoV-2 infection.

Estimated incidence/hospitalization with SARS-CoV-2 in pregnancy in different population subgroups

|                        | Incidence/1000 pregnant women      | Adjusted Odds Ratio (95% CI) |
|------------------------|------------------------------------|------------------------------|
| Black                  | 28.4 black vs 3.5 white            | 8.1 (6.2-10.5)               |
| Age ≥35 years          | 8.8 age ≥35 yr vs 3.9 age 20-34 yr | 2.3 (1.8-2.7)                |
| BMI 25-30 - overweight | 6.8 BMI 25-30 vs 3.5 BMI <25       | 2.0 (1.5-2.5)                |
| BMI >30 - obese        | 8.7 BMI ≥30 vs 3.5 BMI <25         | 2.5 (2.0-3.2)                |

#COVID19Series

### More Severe COVID-19 in Pregnant vs Non-Pregnant Women of Reproductive Age: US

Ellington S et al. *MMWR*. 2020 Jun;69:769-75

- Compared severity of COVID-19 disease among 8,207 pregnant and 83,205 non-pregnant women of reproductive age with positive SARS-CoV-2 rtPCR reported to CDC in US January 22-June 7 2020.

Comparison of Outcomes, Pregnant vs Non-Pregnant Women with COVID-19

|                        | Pregnant women (n=8,207) | Non-pregnant women (N=83,205) | Adjusted* Rate Ratio (95% CI) |
|------------------------|--------------------------|-------------------------------|-------------------------------|
| Hospitalization        | 2,587 (31.5%)            | 4,840 (5.8%)                  | 5.4 (5.1-5.6)                 |
| ICU admission          | 120 (1.5%)               | 757 (0.9%)                    | 1.5 (1.2-1.8)                 |
| Mechanical ventilation | 42 (0.5%)                | 225 (0.3%)                    | 1.7 (0.1-2.4)                 |
| Death                  | 16 (0.2%)                | 208 (0.2%)                    | 0.9 (0.5-1.5)                 |

\*Adjusted for age as continuous variable, yes/no for underlying condition, and race/ethnicity; non-pregnant women are referent group.

- Older age risk factor for severity; when stratified by age, all outcomes more frequent among women aged 35-44 years than among those aged 15-34 years.

5.1.2e

#COVID19Series

### More Severe COVID-19 in Pregnant vs Non-Pregnant Women of Reproductive Age: Living Systematic Review

*Allotey J et al. BMJ. 2020 Sept;370:m3320*

- Living systematic review University Birmingham UK – identified 77 papers including 13,118 pregnant women and 83,486 non-pregnant women of reproductive age hospitalized with COVID-19.

Comparison of Outcomes, Pregnant vs Non-Pregnant Women with COVID-19

|                        | No. Studies | Pregnant women   | Non-pregnant women | Odds Ratio (95% CI) |
|------------------------|-------------|------------------|--------------------|---------------------|
| ICU admission          | 4           | 121/8,276 (1.5%) | 758/83,330 (0.9%)  | 1.6 (1.3-2.0)       |
| Mechanical ventilation | 4           | 43/8,276 (0.5%)  | 226/83,330 (0.3%)  | 1.9 (1.4-2.6)       |
| Maternal death         | 4           | 16/8,282 (0.2%)  | 208/83,327 (0.2%)  | 0.81 (0.5-1.3)      |

- Older age ( $\geq 35$  years), high body mass index and pre-existing co-morbidity (hypertension, diabetes) were risk factors for severity of COVID-19 in pregnancy.

5.1.2e

---

#COVID19Series

### What are Requirements for *In Utero* Transmission?

- In utero* infection requires the pathogen to be able to **reach and cross the placenta and to infect the fetus**.
  - Is there **viremia** to enable the virus to reach placenta?
    - Rarely – 21/587 (3.6%) samples, 8 studies;  $\uparrow$  likelihood severe disease
  - Are there receptors for SARS-CoV-2 in the **placenta**?
    - ACE2 & TMPRSS2 found in placenta, late>early, but co-expression may be minimal (other proteases present and could substitute for TMPRSS2).
  - Are there receptors for SARS-CoV-2 in the **fetus** to enable infection of fetus?
    - ACE2 & TMPRSS2 in fetal lung (peak mid-gestation), heart, liver
  - Is there **placental disruption** to allow viral passage *without* placenta infection?
    - Possible due to coagulopathy – in one study, 10/20 placentas showed some evidence of vascular malperfusion or fetal vascular thrombosis.

5.1.2e

**What Are Requirements for Breast Milk Transmission?**

- Postnatal transmission through breastfeeding requires infant exposure to infectious breast milk and infant infection via oral or gastrointestinal route.
- Has SARS-CoV-2 been detected by rtPCR in breast milk?
- Rarely - 20/196 milk samples (10%) from 10/85 women (12%) positive by PCR, generally transiently, in 12 studies
- If so, is the virus infectious?
- No replication-competent virus in 1 + PCR milk sample (Chen et al. JAMA. 2020 Aug 08)
- 2 cases of infants fed +PCR milk, uninfected (Bianchi et al. Pediatrics 2020)
- 2 cases of infant fed +PCR milk, infected while breastfeeding, but mother infected postpartum, horizontal tx cannot be excluded (Grob et al. Lancet 2020 May 21; Bhargava et al. Lancet 2020 Jun 20)

**#COVID19Series**

**Living Systematic Review: Potential SARS-CoV-2 Vertical Transmission Cases**

- Preliminary review (May 28) – 87 papers including 869 infants
- 52/869 with suspect infection (6.0%): 49 positive rtPCR on respiratory secretions, 3 infants reported with IgM found in neonatal blood.
- However, major issues in most of these papers – for example:
  - Timing of maternal infection (25% first diagnosed postpartum)
  - Type sample ("throat" vs nasopharyngeal vs not specified)
  - Timing of infant testing (many done several days after birth)
  - Lack of confirmatory testing
  - Lack of placental/amniotic fluid testing
  - Lack of serologic testing in the virologic-positive children