Patient Characteristics Associated with SARS-CoV-2 Infection in Parturients Admitted for Labor and Delivery in Massachusetts: A Prospective Cohort Study

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Abstract

Objective: Little is known about the demographic and clinical factors associated with SARS-CoV-2 infection in pregnant women in the United States. The objective of this study was to evaluate the factors associated with SARS-CoV-2 infection in women admitted for labor and delivery, in the context of universal screening. Design: Prospective cohort study. Setting: Four Boston-area hospitals. Population: Convenience sample of all women admitted for delivery (n= 1,153). Methods: We reviewed the health records of all women admitted for delivery at the largest health system in Massachusetts between April 19-May 16, 2020. Factors evaluated for potential association with SARS-CoV-2 infection included age, BMI, race, co-morbidities, zip code, infection in a household member, number of children in the household, occupation, and insurance type. Main Outcome Measures: Risk of SARS-CoV-2 infection and associations between SARS-CoV-2 infection and clinical characteristics. Results: A total of 32 patients (2.8%, 95% confidence interval 1.9-3.9) tested positive for SARS-CoV-2 infection on admission for delivery; 24 (75.0%) of the patients who tested positive were asymptomatic. Factors associated with SARS-CoV-2 infection included: younger age, obesity, African-American or Hispanic race/ethnicity, residence in heavily affected communities, household member with known infection, essential worker occupation, and Medicaid insurance. 93.5% of patients testing positive for SARS-CoV-2 had one or more factors associated with disease acquisition. Conclusions: In this large sample of deliveries, SARS-CoV-2 infection was largely concentrated in patients with distinct demographic characteristics. Understanding factors associated with infection may inform public health efforts directed towards at risk populations and serve in counseling pregnant women.

Introduction

With over 1,500 documented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases per 100,000 residents as of June 22, 2020,[1] the Commonwealth of Massachusetts has the third highest rate of infection per capita in the United States.[2] Mass General Brigham is the largest network of hospitals in Massachusetts. All birth hospitals within the network implemented universal SARS-CoV-2 testing of all women admitted for labor and delivery using polymerase chain reaction (PCR) testing for SARS-CoV-2 on April 19, 2020.

While studies from large cities affected by coronavirus disease 2019 (COVID-19), including this population, have reported on the prevalence of SARS-CoV-2 in the context of universal testing during admission for delivery, little is known about the patient demographic, social, and clinical factors associated with SARS-

CoV-2 infection in pregnant women in the United States.[3-9] Understanding factors associated with SARS-CoV-2 infection at the time of labor and delivery is important for several reasons. First, it can highlight subgroups of pregnant patients who are at particular risk for infection and can inform the counseling of these women throughout pregnancy and as they approach term, with the goal of implementing preventative strategies needed to decrease the risk of infection. Second, in settings where universal rapid testing is limited or not available, it can be used to direct prevention efforts and inform which patients should be prioritized for testing and the types of precautions that should be used while testing is pending.

The aim of this study was therefore to determine the prevalence of, and factors associated with, SARS-CoV-2 infection in patients admitted for labor and delivery at four Boston-area hospitals.

Methods

Mass General Brigham Institutional Review Board approval was obtained for this study, and the need for informed consent was waived (Protocol #2020P001079). Universal testing of all patients admitted for labor and delivery at all Mass General Brigham hospitals began on April 19, 2020. Mass General Brigham includes four large hospitals: two academic medical centers and two community hospitals with a combined estimated annual delivery volume of approximately 15,000 deliveries per year. All women who were admitted for labor and delivery at all Mass General Brigham hospitals between April 19, 2020 and May 16, 2020 and tested for SARS-CoV-2 up to 48 hours before admission or upon admission were included in this study. All SARS-CoV-2 testing was performed by nasopharyngeal reverse transcription-PCR (RT-PCR) using assays approved via United States Food and Drug Administration Emergency Use Authorization. Electronic health records were reviewed for all patients admitted to labor and delivery during the study period to abstract SARS-CoV-2 test results, demographic data, and medical variables that may be associated with SARS-CoV-2 infection.

We calculated the risk (and exact 95% confidence interval) of a positive SARS-CoV-2 test up to 48 hours before or on admission to labor and delivery among our study population over the entire study population and by study week. Patients not tested for SARS-CoV-2 were excluded from these analyses, as were patients who tested positive earlier in pregnancy but negative at the time of admission for labor and delivery, given the focus of the study was on the risk of SARS-CoV-2 infection at the time of delivery. We calculated the percentage of women testing positive for SARS-CoV-2 on admission who were asymptomatic, with symptoms defined as fever, chills, cough, dyspnea, myalgia, headache, anosmia, ageusia, sore throat, rhinorrhea, nausea or vomiting, abdominal pain, and diarrhea. The average daily positive tests per 100 admissions to labor and delivery were compared to statewide data from the Massachusetts Department of Public Health per 100,000 residents aged 20-39 by study week.

Demographic, socio-economic and clinical factors evaluated for their association with infection included maternal age, body mass index (BMI), race, co-morbidities (gestational diabetes, preexisting diabetes, asthma, smoking, opioid use disorder), zip code, known SARS-CoV-2 infection in a household member, parity (as a surrogate for number children in the household), occupation, and insurance type (MassHealth or Medicaid vs. commercial insurance). We identified the factors most strongly associated with SARS-CoV-2 infection and determined the risk of infection, stratified based on the number of factors associated with infection present.

The zip code of patient residence was mapped to the corresponding towns.[10] The COVID-19 rate, defined as the number of confirmed cases per capita provided from the Massachusetts Department of Public Health,[1] was recorded on May 13, 2020. Occupation for each patient was classified into categories based on the United States Bureau of Labor Statistics 2018 Standard Occupation Classification System.[11] Occupations were then classified as essential workers vs. nonessential workers, with healthcare workers being a subset of essential workers. Occupations were determined to be essential based on the emergency order enacted by the governor of Massachusetts on March 23, 2020;[12] those included as essential were: building and grounds cleaning and maintenance occupations, food preparation and serving related occupations, healthcare practitioners and technical occupations, healthcare support occupations, installation, maintenance, and repair occupations, military support occupations, protective service occupations, and transportation and material moving occupations. The medical records of all essential workers were manually searched for documentation of whether the patient was working from home or not working. If patients whose job fell into the essential workers category were specifically noted to be working from home or not working for over two weeks prior to delivery, they were not included in the essential worker category.

Due to the limited number of SARS-CoV-2 infections, estimating a full multivariable logistic regression model including all covariates of interest was not feasible.[13] Therefore, a set of simple logistic regression models was used to assess the univariate association between each covariate of interest and the odds of SARS-CoV-2 infection. As an exploratory analysis, multivariable logistic regression with the least absolute shrinkage and selection operator (lasso)[14]was used to identify a small subset of predictors with the strongest association with SARS-CoV-2 infection. Lasso is a penalized regression method that constrains the sum of the magnitude of regression model coefficients such that covariates that do not improve prediction of the outcome are shrunk to zero, thus creating a more parsimonious model.[15] The degree of penalization, lambda, was selected as the largest value that maintained 10-fold cross-validated prediction error within 1 standard error of the minimum.[14] The risk of SARS-CoV-2 infection and corresponding 95% confidence intervals were estimated amongst subgroups of patients using Poisson regression with robust error variance. Missing data on race (9.9%), occupation category (7.6%), and delivery BMI (0.2%) were addressed using multiple imputation by fully conditional specification, assuming that data were missing at random given observed data.[16] Specifically, predictive mean matching, logistic regression, and the discriminant function method were used to impute continuous variables, binary and ordinal categorical variables, and nominal categorical variables, respectively, to create 20 complete datasets. Imputation models included all predictors assessed for univariate association with SARS-CoV-2 infection, as well as delivery hospital and SARS-CoV-2 test result. Odds ratio and risk estimates with corresponding standard errors were obtained from each of the 20 complete datasets and combined using Rubin's rules to produce pooled estimates with 95% confidence intervals.[17] Lasso selected the same set of predictors across all imputations, and final coefficients were obtained by averaging across imputations. A complete case analysis was performed as a sensitivity analysis. Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC, USA) and R software version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

There were 1,153 deliveries at Mass General Brigham hospitals during the study time period. Four patients who were not tested for SARS-CoV-2 and six who tested positive earlier in pregnancy but negative at the time of admission for labor and delivery were excluded from all analyses; 22 patients residing outside Massachusetts were excluded from any analysis assessing COVID-19 rate by zip code (Figure 1). Thirty-two out of 1,143 women tested positive for SARS-CoV-2 on admission; the risk of SARS-CoV-2 infection of patients tested in our sample was 2.8% (95% confidence interval [CI], 1.9-3.9). In Figure 2, new positive tests per capita in our study are compared to age-specific statewide data from the Massachusetts Department of Public Health by study week, with both populations showing a gradual decline in cases over the four-week study period.

Demographic and clinical factors strongly associated with SARS-CoV-2 infection include younger age (OR 4.01, 95% CI 1.55-10.41 for age <25 compared to age 25-35), obesity (OR 3.26, 95% CI 0.76-14.03 for delivery BMI > 30.0 kg/m^2 compared to < 24.9 kg/m^2), African American race (OR 6.54, 95% CI 1.96-21.85), and Hispanic ethnicity (OR 19.87, 95% CI 7.72-51.13) (Table 1; complete case analysis, Appendix 1). Geographic and occupational factors strongly associated with infection include an increased rate of documented SARS-CoV-2 infections per capita in the patient's town (OR 26.85, 95% CI 7.86-91.66 for$> 95^{th}$ percentile compared to$< 90^{th}$), a household member with known SARS-CoV-2 infection (OR 31.81, 95% CI 13.37-75.65), essential worker occupation excluding healthcare workers (OR 7.33, 95% CI 3.16-16.99), and Medicaid insurance vs. commercial (OR 10.87, 95% CI 5.14-22.98) (Table 2; complete case analysis, Appendix 1).

93.5% of women who tested positive at the time of admission for labor and delivery had at least one of these factors strongly associated with SARS-CoV-2 infection; 54.8% had four or more identifiable factors (Table 3, Figure 3). In contrast, only 5.8% of patients testing negative for SARS-CoV-2 had four or more factors associated with infection. While the number of outcome events precluded assessing the independent effect of each of these factors, the lasso regression identified COVID-19 rate in the 95^{th}-99^{th} percentile, Hispanic ethnicity, household member with known SARS-CoV-2 infection, and MassHealth or Medicaid insurance as the strongest predictors (Appendix 2). Among women testing positive on admission for labor and delivery, 75.0% were asymptomatic (Table 4).

Discussion

Main Findings

In this large sample of patients admitted for labor and delivery undergoing universal SARS-CoV-2 testing during the height of the initial surge of infections in Massachusetts, we observed an overall 2.8% risk of infection, with three-quarters of infected patients being asymptomatic. The risk was largely clustered in patients with distinct demographic and occupational characteristics.

The risk of infection was 12% for women living in the towns most heavily affected by COVID-19 based on publicly reported case rates in the general population, compared to 0.5% for those living in towns with the lowest infection rates. Approximately 14% of Hispanic women and 5% of African American women were infected, versus 0.8% of Caucasian and Asian women. The risk of infection in public health beneficiaries was more than ten-fold higher than in privately insured women. Essential workers outside of healthcare had a markedly high risk of infection, 14%. Furthermore, 93.5% of patients with SARS-CoV-2 infection had at least one of six factors associated with infection; over half had four or more.

The factors associated with SARS-CoV2 infection may vary between communities and are likely to evolve as the pandemic progresses in various settings. Based on Massachusetts data at the peak of the spring 2020 surge, the strong association of infection with particular demographic characteristics and neighborhoods suggest the need for public health officials and clinicians to track and use this type of data as outbreaks occur in order to implement interventions aimed at decreasing infection rates in particular communities.[18] The high risk of infection in non-healthcare essential workers suggests that directive work-related precautions should be offered to women who work in non-healthcare related high risk settings, if at all possible. As having a household member with known SARS-CoV-2 infection was also strongly associated with infection at the time of admission for labor and delivery, all household members should be counseled to take precautions to avoid infection, which may prevent transmission of the virus to the parturient. Risk stratification of patients at risk for SARS-CoV-2 infection is also instructive at the hospital level. Some hospitals may not have the capacity to test all parturients or may not have rapid SARS-CoV-2 testing available, leading to a need to prioritize patients at highest risk for infection for testing.

Our data demonstrate that pregnant women from vulnerable populations were disproportionately affected by SARS-CoV2 infection during the first wave of infection in Massachusetts. These trends are in line with the widespread racial and socioeconomic disparities in COVID-19 seen in the general population in several geographic areas, and though explanations for these disparities are multifold, it is likely that residence in crowded urban settings, poverty and employment in essential occupations, and decreased access to care play a role.[19,20] Thus, there are profound racial and economic disparities in COVID-19 in pregnant women in Massachusetts that track racial and economic disparities in maternal health and obstetrical outcomes observed more generally.[21]

Compared to data from our study, the documented rates of new SARS-CoV-2 infection per capita in the state of Massachusetts for the people aged 20-39 was multi-fold lower,[1] likely due to a substantial undercounting of disease burden given widespread asymptomatic disease and limited testing available for the general population. Most SARS-CoV-2 testing is performed due to patient symptoms; there are few settings where ongoing universal screening of otherwise healthy patients is conducted. Thus, such universal testing can provide valuable insight into the disease dynamics in the community and can be used to monitor the burden of disease.[3-6]

Strengths and Limitations

Strengths of our study include the high rate (>99%) rate of SARS-CoV-2 testing on admission, with a large study population of over 1,000 patients included in a four-week time period. Furthermore, manual chart review of all patients allowed for robust examination of detailed demographic and clinical data. With 32 cases of infection in our sample, it was not possible to perform extensive multivariable adjustments, particularly given that a number of factors associated with infection may be correlated, but an understanding of the factors associated with infection remains relevant to recognizing which patients may be at risk for SARS-CoV-2 infection. Moreover, the linear relationship of risk of infection with each additional associated factor suggests that the factors are not all correlated and that there is additive risk with each added factor. In this study, we equate a negative test with the lack of infection, but while the sensitivity of the test is high, it may be imperfect. However, in the context of an overall low prevalence of infection, false negatives are unlikely to substantially bias the associations with risk factors reported. Finally, the frequencies of SARS-CoV-2 infection in pregnant patients and factors associated with infection may not be fully generalizable to the general population, given physiologic changes specific to pregnancy and potential variations in behavior of pregnant women compared to the general population, particularly in the weeks leading up to delivery. Nonetheless, our findings remain important in risk stratifying parturients at risk for SARS-CoV-2 infection throughout pregnancy and at the time of labor and delivery and in directing counseling and prevention efforts.

Conclusion

In summary, in our large cohort of women admitted for labor and delivery in Massachusetts undergoing universal SARS-CoV-2 infection screening, there were multiple identifiable factors associated with infection. Almost all patients who tested positive for infection had one or more identifiable factors associated with disease. SARS-CoV-2 infection most heavily affected pregnant women who were younger, African American or Hispanic, non-healthcare essential workers, publicly insured, or from heavily affected areas, underscoring another source of disparity in obstetrics.

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Contributions to Authorship:

SR helped in the conception, planning, carrying out, analyzing and writing up of the manuscript. MLM helped in the conception, planning, carrying out, analyzing and writing up of the manuscript. CK helped in the planning and carrying out of the manuscript. SB helped in the planning and carrying out of the manuscript. KF helped in planning, carrying out, analyzing and writing up of the manuscript. KD helped in planning, analyzing and writing up of the manuscript. IG helped in planning, analyzing and writing up of the manuscript. AC helped in planning, analyzing and writing up of the manuscript. JR helped in the conception, planning, and writing up of the manuscript. KG helped in the conception, planning, and writing up of the manuscript. KH helped in the conception, planning, carrying out, analyzing and writing up of the manuscript. BB helped in the conception, planning, carrying out, analyzing and writing up of the manuscript.

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Table 1: Demographics and Clinical Factors Associated with SARS-CoV-2 infection.

	SARS-CoV-2 infection	SARS-CoV-2 infection	
	Positive n=32	Negative n=1111	Odds ratio, 95% confidence interval
Maternal age, years, mean ± SD	28.8 ± 6.1	32.8 ± 4.8	
Age <25, n (%)	6 (18.8)	56 (5.0)	4.01 (1.55 - 10.41)
Age 25-35, n (%)	20 (62.5)	749 (67.4)	Reference
Age >35, n (%)	6 (18.8)	306 (27.5)	0.73 (0.29 - 1.85)
BMI, kg/m^2, mean ± SD	33.3 ± 6.1	30.7 ± 6.0	
Normal (< 24.9 kg/m^2), n (%)	2 (6.3)	156 (14.1)	Reference
Overweight (25.0 - 29.9 kg/m^2), n (%)	8 (25.0)	426 (38.4)	1.47 (0.31 - 6.98)*
Obese (> 30.0 kg/m^2), n (%)	22 (68.8)	527 (47.5)	3.26 (0.76 – 14.03)*
Race/Ethnicity, n (%)			
African American	5 (15.6)	94 (8.6)	6.54 (1.96-21.85)*
Asian	1 (3.1)	122 (11.1)	1.01 (0.12-8.49)*
Caucasian	6 (18.8)	744 (67.8)	Reference
Hispanic	18 (56.3)	112 (10.2)	19.87 (7.72-51.13)*
Other	2 (6.3)	26 (2.4)	9.53 (1.84-49.48)*
Comorbidities, n (%)			
Gestational diabetes	1 (3.1)	99 (8.9)	0.33 (0.04-2.45)
Preexisting diabetes	0 (0.0)	6 (0.5)	N/A+
Asthma	6 (18.8)	123 (11.1)	1.85 (0.75-4.60)
Tobacco exposure	0 (0.0)	11 (1.0)	N/A+
Opioid use disorder	0 (0.0)	12 (1.1)	N/A+

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2; SD = Standard deviation; BMI = Body mass index; kg = Kilogram; m^2 = Square meter; N/A = Not applicable

* Missing data

+ Odds ratio could not be calculated due to zero prevalence of factor in SARS-CoV-2 positive patients

Table 2: Geographic and Occupational Factors Associated with SARS-CoV-2 infection.

	SARS-CoV-2 Testing	SARS-CoV-2 Testing	
	Positive n=32	Negative n=1111	Odds ratio, 95% confidence interval

	SARS-CoV-2 Testing	SARS-CoV-2 Testing	
Percentile, COVID-19 rate among Massachusetts towns (based on cases/100,000 residents)			
<90$^{\text{th}}$, n (%)*	3 (9.4)	600 (55.1)	Reference
90-94$^{\text{th}}$, n (%)+	9 (28.1)	340 (31.2)	5.29 (1.42 - 19.72)
>95$^{\text{th}}$, n (%)++	20 (62.5)	149 (13.7)	26.85 (7.86 - 91.66)
Household member with known SARS-CoV-2 infection, n (%)	11 (34.4)	18 (1.6)	31.81 (13.37-75.65)
Number of children at home, median (Q1, Q3)	0.5 (0, 2)	1 (0, 1)	0.86 (0.43-1.75)§
Occupation, n (%)			
Nonessential workers	19 (61.3)	836 (81.6)	Reference
Healthcare workers	3 (9.7)	135 (13.2)	0.98 (0.29-3.35)‖
Essential workers excluding healthcare workers	9 (29)	54 (5.3)	7.33 (3.16-16.99)‖
Insurance type, n (%)			
MassHealth or Medicaid	21 (65.6)	166 (14.9)	10.87 (5.14-22.98)
Commercial or out of pocket	11 (34.4)	945 (85.1)	Reference

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2; COVID-19 = Coronavirus disease 2019; Q1 = First quartile; Q3 = Third quartile

* 0-1,1436 cases/100,000 residents

+ 1,437-1,791 cases/100,000 residents

++ 1,792-6404 cases/100,000 residents

§ [?]1 vs. 0 children at home

‖ Missing data

Table 3: Risk of SARS-CoV-2 infection stratified by patient characteristics.

	Positive n	Total n	Risk of SA
Maternal age			
Age <25	6	62	9.7 (4.5-20
Age 25-35	20	769	2.6 (1.7-4)
Age >35	6	312	1.9 (0.9-4.
BMI			
Normal (< 24.9 kg/m^2)	2	158	1.3 (0.3-5.
Overweight (25.0 - 29.9 kg/m^2)	8	434	1.8 (0.9-3.
Obese (> 30.0 kg/m^2)	22	549	4.0 (2.7-6.

	Positive n	Total n	Risk of SA
Race/ethnicity			
African American	5	99	5.0 (2.1-1
Asian	1	123	0.8 (0.1-5.
Caucasian	6	750	0.8 (0.4-1.
Hispanic	18	130	13.7 (8.9-2
Other	2	28	7.1 (1.8-2
COVID-19 rate category among Massachusetts towns (based on cases/100,000 residents)			
<90th	3	603	0.5 (0.2, 1
90-94th	9	349	2.6 (1.4, 4
>95th	20	169	11.8 (7.8,
Household member with known SARS-CoV-2 infection			
Yes	11	29	37.9 (23.8
No	21	1114	1.9 (1.2-2.
Occupation			
Nonessential workers	19	855	2.1 (1.3-3.
Healthcare workers	3	138	2.1 (0.7-6.
Essential workers excluding healthcare workers	9	63	13.5 (7.4-2
Insurance type			
MassHealth or Medicaid	21	187	11.2 (7.5-1
Commercial or out-of-pocket	11	956	1.2 (0.6-2.

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2; CI = Confidence interval; BMI = Body mass index; kg = Kilogram; m^2 = Square meter; COVID-19 = Coronavirus disease 2019

* Missing data

Table 4: Characteristics of SARS-CoV-2 Positive Patients.

	n=32
Asymptomatic on admission, n (%)	24 (75)
Symptoms, n (%)	
Fever	5 (15.6)
Chills	1 (3.1)
Cough	4 (12.5)
Dyspnea	4 (12.5)
Myalgia	3 (9.4)
Headache	2 (6.3)
Anosmia	4 (12.5)
Ageusia	2 (6.3)
Sore throat	2 (6.3)
Rhinorrhea	2 (6.3)
Nausea or vomiting	1 (3.1)
Abdominal pain	1 (3.1)
Diarrhea	1 (3.1)
Cesarean delivery, n (%)	14 (43.8)
Gestational age at delivery, weeks, mean ± SD	38.6 ± 2.2

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2; SD = Standard deviation

Figure Legends

Figure 2

- X axis: Study week.
- Y axis: Average daily new coronavirus disease 2019 (COVID-19) cases per 100 admissions to Mass General Brigham Hospital Labor and Delivery with 95% confidence intervals vs. average daily new COVID-19 cases per 100,000 Massachusetts residents.

Figure 3

- X axis: Number of factors associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Factors included in analyses: age <25, body mass index (BMI)> 30 kg/m^2, African American or Hispanic race/ethnicity, coronavirus disease 2019 (COVID-19) rate in the patient's town > 95^{th}percentile, household member with known SARS-CoV-2 infection, essential worker occupation (excluding healthcare worker), and MassHealth or Medicaid insurance. Number of infected patients in each category: 0 factors associated with infection, 2 patients; 1 factor, 1 patient; 2 factors, 6 patients; 3 factors, 5 patients; 4 factors, 10 patients; 5+ factors, 7 patients.
- Y axis: Risk of SARS-CoV-2 infection with error bars representing 95% confidence intervals for the risks.

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