**Introduction:**

Since December 2019, there have been over 760 million confirmed cases, and over 6.5 million deaths, due to SARS-CoV-2 during the COVID-19 pandemic.1 The impacts of this novel coronavirus have necessitated the need to broaden our scientific understandings of how such viruses can affect human populations. One key area of concern was how COVID-19 infection could uniquely affect pregnant individuals and their neonates. A continually growing area of research, we have found mixed results on COVID-19’s impact on maternal and child health during pregnancy, especially in different world areas.

Several studies have examined the effects of SARS-CoV-2 infection on pregnancy outcomes. One Turkish study found that mothers infected with COVID-19 experienced higher rates of maternal mortality, preterm birth, and cesarean section delivery.2 One review article summarized that COVID-19 infections in pregnant mothers have been associated with preeclampsia, preterm birth, and stillbirth, and that these effects (plus low birthweight) are stronger in cases of severe COVID-19 infection.3

Air pollution is a pressing environmental challenge which can have disastrous consequences on the climate and on human health. Particulate matter (PM) sources are classified by their size, where PM2.5 have a diameter less than 2.5 μm, and PM10 have a diameter less than 10 μm. Both PM2.5 and PM10 are known to be associated with adverse respiratory health outcomes, including pneumonia and lung disease.4–6 Besides PM, gases like nitrogen oxides, ammonia, ozone, sulfur dioxides, and carbon monoxides also contribute to air pollution. Prolonged exposure to increased concentration of nitrogen dioxide has been linked to harmful and toxic effects on the respiratory system.4,6,7

Air pollution may exacerbate health outcomes of COVID-19. Several studies in the United States have suggested that long-term exposure to PM2.5 is associated with COVID-19 infection,8 hospitalization,9,10 mortality,8 and fatality8; in addition, another US-based study found that long-term and short-term PM2.5 and NO2 exposure was associated with higher COVID-19 incidence.11 Exposure to air pollution has negatively impacted the COVID-19 pandemic outside of the United States as well. Daily increases in air pollution have been positively correlated with COVID-19 mortality in Chile,12 PM2.5 and NO2 exposure have been linked to COVID-19 incidence in China,13 PM2.5 and PM10 exposure have been positively associated with COVID-19 incidence and mortality in Germany,14 and PM2.5, PM10, and NO2 exposure were positively associated with COVID-19 incidence in India.15

Air pollution may have negative impacts during pregnancy as well. Previous studies have suggested that PM10 exposure increased risk of spontaneous abortion, and that PM10 and PM2.5 exposure in the third trimester increased the risk of stillbirth.16 Also, exposure to PM and ozone throughout pregnancy may increase the risk of preterm birth.17,18

While both COVID-19 and exposure to air pollution can have detrimental health impacts during pregnancy, scientific literature has insufficiently examined the synergistic impacts of COVID-19 and air pollution on pregnancy health outcomes. In fact, only one paper by Casey, et al. (2022) has examined these three variables (air pollution, COVID-19, and pregnancy) simultaneously.19 In this paper, we will examine the joint impacts of COVID-19 infection and air pollution exposure during the third trimester on pregnancy outcomes in a New York City cohort. Based on what is known from the current scientific literature, we hypothesize that COVID-19 infection and air pollution together will have a stronger impact on adverse pregnancy outcomes than they will alone.

**Methods**

Our study participants included all pregnant individuals who gave birth in New York City between March 2020 and February 2021 in the following health systems: Albert Einstein School of Medicine/Montefiore Medical Center, Columbia University and Weill Cornell Medicine/New York-Presbyterian Hospital, Icahn School of Medicine/Mount Sinai Health System, and New York University School of Medicine/Langone Medical Center.

*Data Sources*

Patient demographic and health information was obtained via electronic medical records from each institution. Only the average air pollution exposure and neighborhood vulnerability index variables did not come from electronic medical records.

Long-term air pollution was represented by a 10-year averaged PM2.5 exposure variable, gathered from the New York City Community Air Survey (NYCCAS).20

Neighborhood vulnerability index (NEVI) was constructed for each NYC residential zip code tabulation area (ZCTA) using the toxicological prioritization index (ToxPi) profiling and clustering approach; these methods have been described elsewhere.21 Our constructed NEVI included only neighborhood-level social, economic, and chronic disease factors. Air pollution metrics were not included in the construction of the NEVI to allow us to examine the direct effects of socioeconomic factors, separate from the effects of air pollution.

*COVID-19 Infection Assessment*

During the study time period, universal SARS-CoV-2 nasopharyngeal quantitative polymerase chain reaction (PCR) testing was performed at delivery for every patient giving birth in New York City. The electronic medical record contained information whether these patients tested positive or negative for SARS-CoV-2 at the time of delivery.

*Air Pollution Exposure*

Air pollution data was obtained from the NYCCAS. We represented long-term air pollution using a 10-year averaged PM2.5 exposure level. Participants were assigned an average PM2.5 level based on their zip code of residence at the time of delivery. The continuous averaged air pollution variable was then split into quartiles. This categorical variable was used in all analyses.

*Birth Outcomes*

Our outcomes of interest in this study were delivery type (cesarean or vaginal) and pre-eclampsia status to represent hypertension during pregnancy. While we were interested in examining the impact of COVID-19 infection and air pollution on stillbirth and maternal mortality as well, the low rates of these adverse birth outcomes in our study population contributed to an underpowered analysis—these outcomes were consequently dropped.

*Covariates*

We created a directed acyclic graph to hypothesize potential confounders (Figure 1). We used a minimally sufficient adjustment set for estimating the total effect of COVID-19 infection on delivery type and pre-eclampsia status. These covariates included diabetes status, asthma status, ever-smoker status, maternal age at birth, and the NEVI.

*Statistical Analysis*

We performed multivariate logistical regression models to examine the effects of COVID-19 infection and long-term air pollution on each of the two birth outcomes. Because the effects of SARS-CoV-2 have been distinct based on circulating variants, all analyses were stratified on the wave of the pandemic during which patients gave birth. We defined the first wave to be from March 2020 to June 2020, the second wave to be from July 2020 to October 2020, and the third wave to be from November 2020 to February 2021.

We modeled the effects of COVID-19 infection on delivery type and pre-eclampsia status in crude models, then separately added an interaction term to test for effect modification by the categorical air pollution variable. Adjusted models included the following covariates: asthma status (yes/no), diabetes status (defined as having any diabetes diagnosis in the medical record), maternal age at birth, and the constructed NEVI. We reported odds ratios and 95% confidence intervals for these effects. To report any effect modification between air pollution and COVID-19 infection, we used linear combination to report the effect of COVID-19 infection in the second, third, and fourth quartile of air pollution exposure, compared to the effect of COVID-19 infection alone.

*Ethics/ Role of the Funding Source/ Data Availability*

**TABLES AND FIGURES**

Chart

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Diagram

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**Table 1. Patient Characteristics**

| **Variable** | **N = 6,703**1 |
| --- | --- |
| Age | 32 (28, 36) |
| Ethnicity |  |
| Latina/Hispanic | 1,838 (27%) |
| Non-Latina/Non-Hispanic | 4,865 (73%) |
| Race |  |
| Unknown | 195 (2.9%) |
| American Indian or Alaska Native | 21 (0.3%) |
| Asian | 659 (9.8%) |
| Black | 780 (12%) |
| Declined | 265 (4.0%) |
| Multiple Race | 338 (5.0%) |
| Native Hawaiian or Other Pacific Islander | 73 (1.1%) |
| Other | 1,270 (19%) |
| White | 3,102 (46%) |
| COVID-19 Status at Delivery |  |
| COVID-19 Infection | 1,332 (20%) |
| No COVID-19 Infection | 5,371 (80%) |
| Delivery Type |  |
| C-Section | 1,175 (18%) |
| Vaginal Delivery | 5,528 (82%) |
| Pre-eclampsia Status |  |
| No Pre-eclampsia | 6,089 (91%) |
| Pre-eclampsia | 614 (9.2%) |
| Stillbirth Status |  |
| Live Birth | 6,644 (99%) |
| Stillbirth | 59 (0.9%) |
| Single/multiple gestation |  |
| Multiple Gestation | 119 (1.8%) |
| Singleton | 6,584 (98%) |
| Maternal Mortality |  |
| Mother Alive | 6,685 (100%) |
| Unknown | 18 |
| Asthma Status |  |
| Asthma | 703 (10%) |
| No Asthma | 6,000 (90%) |
| Diabetes Status |  |
| Diabetes | 164 (2.4%) |
| No Diabetes | 6,539 (98%) |
| Smoking Status |  |
| Ever Smoker | 196 (2.9%) |
| Non-Smoker | 6,507 (97%) |
| Date of Delivery |  |
| Wave 1 (March 2020 - June 2020) | 1,513 (23%) |
| Wave 2 (July 2020 - October 2020) | 2,578 (38%) |
| Wave 3 (November 2020 - February 2021) | 2,612 (39%) |
| Average PM Score in Zip Code of Residence | 9.02 (8.30, 9.66) |
| Unknown | 2,328 |
| NEVI in Zip Code of Residence | 0.35 (0.31, 0.41) |
| Unknown | 2,361 |
| Quartiles of Average PM Score |  |
| 1 | 1,094 (25%) |
| 2 | 1,094 (25%) |
| 3 | 1,094 (25%) |
| 4 | 1,093 (25%) |
| Unknown | 2,328 |
| 1Median (IQR) or Frequency (%) |  |

**Table 1a. Patient Characteristics during Wave 1**

| **Characteristic** | **N = 1,513**1 |
| --- | --- |
| Age | 32.0 (27.0, 36.0) |
| Ethnicity |  |
| Latina/Hispanic | 588 (39%) |
| Non-Latina/Non-Hispanic | 925 (61%) |
| Race |  |
| Unknown | 80 (5.3%) |
| American Indian or Alaska Native | 4 (0.3%) |
| Asian | 107 (7.1%) |
| Black | 208 (14%) |
| Declined | 59 (3.9%) |
| Multiple Race | 139 (9.2%) |
| Native Hawaiian or Other Pacific Islander | 12 (0.8%) |
| Other | 322 (21%) |
| White | 582 (38%) |
| COVID-19 Status at Delivery |  |
| COVID-19 Infection | 695 (46%) |
| No COVID-19 Infection | 818 (54%) |
| Delivery Type |  |
| C-Section | 362 (24%) |
| Vaginal Delivery | 1,151 (76%) |
| Pre-eclampsia Status |  |
| No Pre-eclampsia | 1,339 (88%) |
| Pre-eclampsia | 174 (12%) |
| Stillbirth Status |  |
| Live Birth | 1,495 (99%) |
| Stillbirth | 18 (1.2%) |
| Single/multiple gestation |  |
| Multiple Gestation | 32 (2.1%) |
| Singleton | 1,481 (98%) |
| Maternal Mortality |  |
| Mother Alive | 1,506 (100%) |
| Unknown | 7 |
| Asthma Status |  |
| Asthma | 178 (12%) |
| No Asthma | 1,335 (88%) |
| Diabetes Status |  |
| Diabetes | 52 (3.4%) |
| No Diabetes | 1,461 (97%) |
| Smoking Status |  |
| Ever Smoker | 78 (5.2%) |
| Non-Smoker | 1,435 (95%) |
| Average PM Score in Zip Code of Residence | 9.17 (8.53, 9.65) |
| Unknown | 484 |
| NEVI in Zip Code of Residence | 0.38 (0.33, 0.43) |
| Unknown | 492 |
| Quartiles of Average PM Score |  |
| 1 | 151 (15%) |
| 2 | 283 (28%) |
| 3 | 345 (34%) |
| 4 | 250 (24%) |
| Unknown | 484 |
| 1Median (IQR) or Frequency (%) |  |

**Table 1b. Patient Characteristics during Wave 2**

| **Characteristic** | **N = 2,578**1 |
| --- | --- |
| Age | 32.0 (28.0, 36.0) |
| Ethnicity |  |
| Latina/Hispanic | 638 (25%) |
| Non-Latina/Non-Hispanic | 1,940 (75%) |
| Race |  |
| Unknown | 71 (2.8%) |
| American Indian or Alaska Native | 11 (0.4%) |
| Asian | 283 (11%) |
| Black | 282 (11%) |
| Declined | 100 (3.9%) |
| Multiple Race | 118 (4.6%) |
| Native Hawaiian or Other Pacific Islander | 28 (1.1%) |
| Other | 457 (18%) |
| White | 1,228 (48%) |
| COVID-19 Status at Delivery |  |
| COVID-19 Infection | 296 (11%) |
| No COVID-19 Infection | 2,282 (89%) |
| Delivery Type |  |
| C-Section | 428 (17%) |
| Vaginal Delivery | 2,150 (83%) |
| Pre-eclampsia Status |  |
| No Pre-eclampsia | 2,340 (91%) |
| Pre-eclampsia | 238 (9.2%) |
| Stillbirth Status |  |
| Live Birth | 2,561 (99%) |
| Stillbirth | 17 (0.7%) |
| Single/multiple gestation |  |
| Multiple Gestation | 44 (1.7%) |
| Singleton | 2,534 (98%) |
| Maternal Mortality |  |
| Mother Alive | 2,573 (100%) |
| Unknown | 5 |
| Asthma Status |  |
| Asthma | 266 (10%) |
| No Asthma | 2,312 (90%) |
| Diabetes Status |  |
| Diabetes | 57 (2.2%) |
| No Diabetes | 2,521 (98%) |
| Smoking Status |  |
| Ever Smoker | 72 (2.8%) |
| Non-Smoker | 2,506 (97%) |
| Average PM Score in Zip Code of Residence | 8.89 (8.28, 9.66) |
| Unknown | 947 |
| NEVI in Zip Code of Residence | 0.34 (0.30, 0.40) |
| Unknown | 959 |
| Quartiles of Average PM Score |  |
| 1 | 482 (30%) |
| 2 | 385 (24%) |
| 3 | 356 (22%) |
| 4 | 408 (25%) |
| Unknown | 947 |
| 1Median (IQR) or Frequency (%) |  |

**Table 1c. Patient Characteristics during phase 3**

| **Characteristic** | **N = 2,612**1 |
| --- | --- |
| Age | 32 (28, 35) |
| Ethnicity |  |
| Latina/Hispanic | 612 (23%) |
| Non-Latina/Non-Hispanic | 2,000 (77%) |
| Race |  |
| Unknown | 44 (1.7%) |
| American Indian or Alaska Native | 6 (0.2%) |
| Asian | 269 (10%) |
| Black | 290 (11%) |
| Declined | 106 (4.1%) |
| Multiple Race | 81 (3.1%) |
| Native Hawaiian or Other Pacific Islander | 33 (1.3%) |
| Other | 491 (19%) |
| White | 1,292 (49%) |
| COVID-19 Status at Delivery |  |
| COVID-19 Infection | 341 (13%) |
| No COVID-19 Infection | 2,271 (87%) |
| Delivery Type |  |
| C-Section | 385 (15%) |
| Vaginal Delivery | 2,227 (85%) |
| Pre-eclampsia Status |  |
| No Pre-eclampsia | 2,410 (92%) |
| Pre-eclampsia | 202 (7.7%) |
| Stillbirth Status |  |
| Live Birth | 2,588 (99%) |
| Stillbirth | 24 (0.9%) |
| Single/multiple gestation |  |
| Multiple Gestation | 43 (1.6%) |
| Singleton | 2,569 (98%) |
| Maternal Mortality |  |
| Mother Alive | 2,606 (100%) |
| Unknown | 6 |
| Asthma Status |  |
| Asthma | 259 (9.9%) |
| No Asthma | 2,353 (90%) |
| Diabetes Status |  |
| Diabetes | 55 (2.1%) |
| No Diabetes | 2,557 (98%) |
| Smoking Status |  |
| Ever Smoker | 46 (1.8%) |
| Non-Smoker | 2,566 (98%) |
| Average PM Score in Zip Code of Residence | 8.92 (8.30, 9.67) |
| Unknown | 897 |
| NEVI in Zip Code of Residence | 0.35 (0.31, 0.40) |
| Unknown | 910 |
| Quartiles of Average PM Score |  |
| 1 | 461 (27%) |
| 2 | 426 (25%) |
| 3 | 393 (23%) |
| 4 | 435 (25%) |
| Unknown | 897 |
| 1Median (IQR) or Frequency (%) |  |

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