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COVID-19 During Pregnancy and Associated Maternal Outcomes Among Race and Ethnicity Groups in Indiana

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Abstract

During 2020 in Indiana, there were 76,467 singleton births. Among those births, 1,625 occurred to people who tested positive for COVID-19 during gestation. Chi-squared tests revealed significant differences in rates of three out of ten adverse maternal outcomes between positive and non-positive groups. These differences were still significant after controlling for age, BMI and educational status using logistic modeling. People with COVID-19 during pregnancy were significantly more likely to have gestational diabetes ($p = 0.002$), give preterm birth ($p = 0.005$) and be admitted to the intensive care unit ($p = 0.003$). Race and ethnicity groups were also analyzed to observe how these associations varied. Black, non-Hispanic people were significantly more likely to give preterm birth ($p = 0.024$) and be admitted to the ICU ($p = 0.009$) if they had COVID-19 while pregnant. These associations seen among the Black, non-Hispanic group likely drove the significance observed for the whole cohort. Hispanic people of any race with COVID-19 while pregnant had a significantly increased chance of being diagnosed with gestational hypertension ($p = 0.017$). No significant associations between COVID-19 and adverse maternal outcomes were found within the White, non-Hispanic or Other, non-Hispanic groups after adjustment for age, BMI and educational status.

Background

Following the outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in December 2019, the World Health Organization (WHO) declared a global pandemic in March 2020. While preceding coronaviruses, SARS-CoV-1 and MERS, just reached the United States with only 8 and 2 confirmed cases, respectively [1, 2], the same cannot be said of COVID-19 (the disease caused by SARS-CoV-2). In Indiana alone, there have been 1,140,151 confirmed cases and 17,310 deaths attributed to COVID-19 as of Dec. 7, 2021 [3].

Coronaviruses and Pregnancy

Pregnant individuals were vulnerable to past SARS and MERS epidemics. Contracting SARS-CoV-1 while pregnant has been associated with severe maternal illness, spontaneous abortion and death [4,5]. Although there have been few cases of MERS in pregnant patients, 91% of those documented cases resulted in adverse clinical outcomes such as emergency cesarean section and maternal death [4]. Recent research from the United States suggests that pregnant individuals with COVID-19 experience higher rates of mortality than their non-pregnant counterparts with COVID-19. In Washington state, the fatality rate among pregnant individuals diagnosed with COVID-19 was 13.6 times higher than that of their non-pregnant counterparts [6]. This association observed in Washington has been supported by the Centers for Disease Control and Prevention (CDC). Pregnant individuals with COVID-19 are significantly more likely to be admitted to intensive care units (ICUs) and to die when compared to similar, non-pregnant individuals [7].

Severity of COVID-19 case has also been associated with several adverse maternal outcomes. In New York City medical centers, pregnant individuals with COVID-19 symptoms such as high respiratory rates or low blood oxygen saturation were significantly more likely to be admitted to the ICU [8] and deliver by cesarean section [9, 10] than people with less severe cases. Similarly in Washington, pregnant individuals with more serious symptoms had an increased incidence of hypertension [6]. These findings on cesarean sections and hypertension were supported by a multistate cohort study [11]. Increased risk of preterm birth has also been associated with more severe cases of COVID-19 in pregnant individuals. [6, 8, 10, 12].

Regardless of case severity, a diagnosis of COVID-19 during pregnancy has been associated with adverse maternal outcomes. Among pregnant individuals in Massachusetts, those who tested positive for COVID-19 delivered pre-term and were diagnosed with pre-eclampsia (a complication of hypertension) at significantly higher rates than those who tested negative [13]. Studies across numerous states have supported these results [14, 15]. These multistate cohort studies also found significant differences between pregnant individuals with and without COVID-19 in rates of cesarean delivery, gestational hypertension, ICU ad-mission and death [14, 15] as well as gestational diabetes [14]. A multinational cohort study has supported the associations observed with all these adverse maternal outcomes, except for gestational diabetes [16].

COVID-19, Pregnancy and Communities of Color in the United States

Historically, systemic barriers have negatively impacted healthcare access and social determinants of health for communities of color in the United States. Research focused on the intersections of race and ethnicity with pregnancy and COVID-19 outcomes has revealed the results of these barriers.

People of color in the United States have disproportionately experienced adverse maternal outcomes. Between 2006 and 2010, Black, non-Hispanic people contributed 14.6% to all live births in the U.S. but accounted for 35.5% of all pregnancy-related deaths. Furthermore, the pregnancy-related mortality rate for Black, non-Hispanic people was higher than that of all other groups, even when adjusted for age [17]. In New York City, between 2010 and 2014, Black and Hispanic pregnancies resulted in significantly higher rates of maternal morbidities than White, non-Hispanic pregnancies. Black, non-Hispanic people were diagnosed with a life-threatening condition or required a life-saving procedure 1.52 times more frequently than White, non-Hispanic people. Similarly,

Hispanic people experienced these same outcomes 1.44 times more frequently. These disparities held true despite adjustments controlling for pre-existing conditions and insurance type [18]. These results are hardly unique. Studies have consistently shown that Hispanic and non-White pregnant individuals experience maternal morbidities significantly more often than their White, non-Hispanic counterparts [19 – 22].

COVID-19 has also had an outsized effect on people of color in the United States. In Indiana, the odds of a positive COVID-19 diagnosis were 4.58 times higher in Black people and 2.58 times higher in Hispanic people when compared to White, non-Hispanic people [23]. Rates of COVID-19 diagnosis, hospitalization after a positive test, ventilator usage once hospitalized and death were all observed to be significantly higher for members of Black and Hispanic communities than for White, non-Hispanic people in New York City [24]. The CDC agrees that these findings reflect widespread trends. In May-August 2020, Black communities bore 18.7% of the deaths attributed to COVID-19 despite accounting for 12.5% of the U.S. populace. During this same time, Hispanic people made up 24.2% of COVID-19 deaths while accounting for 18.5% of the population [25].

Study Objective

Although some research has focused on race and ethnicity as they relate to the maternal outcomes of pregnant individuals with COVID-19 [26, 27], the vulnerability of this group merits further study. Much of the existing research from the United States uses data collected in the Northeast or Northwest regions of the continental U.S. This study aims to investigate the association between COVID-19 and maternal outcomes in pregnant individuals and how that association varies by race and ethnicity groups among singleton births in Indiana during 2020.

Methods

All 50 states and Washington, D.C., report disease data to the CDC through the National Electronic Diseases Surveillance System (NEDSS). In 2003, the CDC implemented the NEDSS Base System (NBS) through which 20 states and six territories, including Indiana, centralized their individual monitoring of certain diseases. As the pandemic evolves, the Indiana Department of Health continues to track COVID-19 cases through NBS. NBS records test results from samples analyzed at in-state medical laboratories. Data from NBS was used in conjunction with Vital Records data to produce the data set for this analysis. Vital Records (VR), which includes information from birth and death certificates, are maintained at the local level for all states and territories throughout the United States. NBS and VR data identified COVID-19 positive people included in this study by matching first names, last names and dates of birth.

Explanatory Variables

People who tested positive for COVID-19 were identified among all recorded live births in Indiana during 2020. Those who gave birth to two or more babies were excluded from analysis in order to remove any confounding effect, given the established association between multiple gestations and adverse maternal outcomes [28 – 30]. To assess the association between COVID-19 and maternal outcomes, only people who tested positive on the day of the birth or during their estimated gestation were classified as positive. Individuals who tested negative, were never tested for COVID-19 or tested positive after their birth event were considered non-positive. To observe how this association varied by race and ethnicity, people were categorized into groups based on their racial and ethnic identity. A person's race and ethnicity would have either been self-reported by that person at the time of their birth event or surmised from previous medical records. The process of determining race and ethnicity likely varied across hospitals and other birthing facilities. The National Center for Health Statistics (NCHS) then finalizes race and ethnicity data before reporting it back to VR. For more information on how race and ethnicities were recorded for this cohort, see Appendix 1. People with Hispanic ethnicity, regardless of their race, made up the Hispanic, any race group in this analysis. White and Black people without Hispanic ancestry were categorized respectively as White, non-Hispanic and Black, non-Hispanic. Asian, American Indian, Native

Alaskan, Native Hawaiian and other Pacific Islander people were grouped together as Other, non-Hispanic for the purposes of this analysis. Certainly, these race groups are distinct from each other, but this group combination was chosen to maintain an appropriate sample size for meaningful analysis. This grouping is discussed further in the limitations section.

Response Variables

Several maternal outcomes were chosen for inclusion. Among outcomes that are frequently covered in comparable literature, this analysis included gestational diabetes, gestational hypertension, preterm birth, cesarean section and ICU admission. Additional adverse maternal outcomes measured were eclampsia, induced labor, abruptio placenta, blood transfusions and unplanned operating room (OR) procedures. Eclampsia is a complication of pre-eclampsia in which the pregnant individual may experience seizures or coma. Abruptio placenta occurs when the placenta separates from the uterine wall before birth, potentially causing heavy bleeding.

Statistical Analysis

The threshold for statistical significance in this analysis was $p \leq 0.05$. Observations that had missing values for any explanatory or response variables were subject to pairwise deletion. Consequently, those people were left out of calculations requiring the missing value. In any calculation, pairwise deleted observations accounted for, at most, 0.01% of the relevant group. To observe the demographics of the cohort, means and 95% confidence intervals (CIs) were calculated for age and Body Mass Index (BMI) before pregnancy. Wald statistics were used to calculate group rates and 95% CIs for both educational status and COVID-19 positivity status (Table 1). Given the established association between race and ethnicity and adverse maternal outcomes, the non-positive group was analyzed to establish trends for maternal outcomes by race and ethnicity for this cohort. Wald statistics were used to produce p-values, and logistic models yielded adjusted odds ratios (aORs) relative to the White, non-Hispanic group (Table 2.) The White, non-Hispanic group was chosen as the reference group because of their established low relative

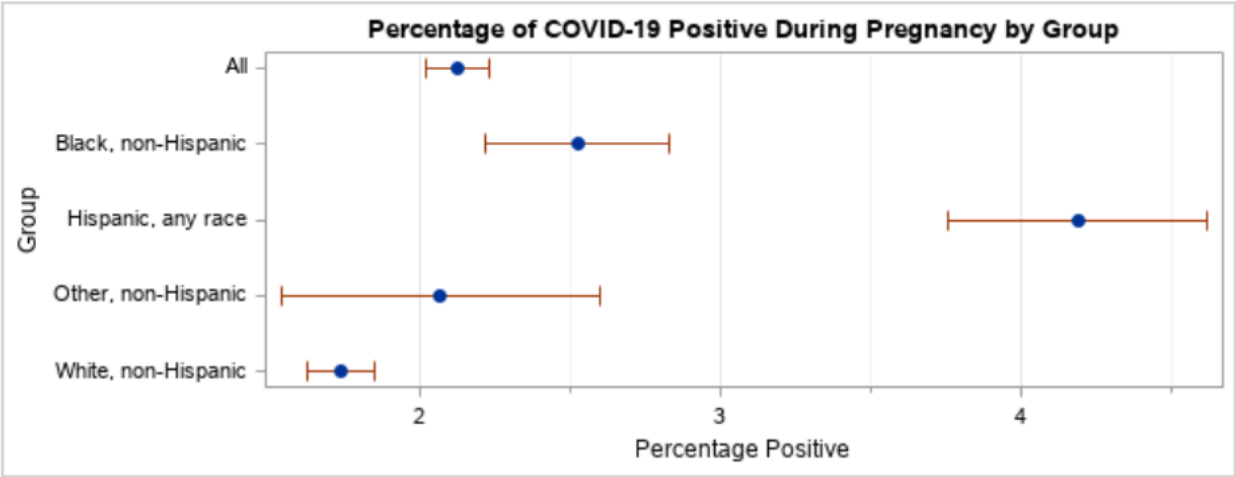
Table 1: Demographics by Race and Ethnicity

Race and Ethnicity	All* (n = 76467)	Black, non-Hispanic (n=10125, 13.3%)	Hispanic, any race (n=8264, 10.8%)	Other, non-Hispanic (n=2801, 3.7%)	White, non-Hispanic (n=55196, 72.3%)
COVID-19 positive during pregnancy percent (95% CI)	2.13 (2.02—2.23)	2.53 (2.22—2.83)	4.19 (3.76—4.62)	2.07 (1.54—2.60)	1.74 (1.63—1.85)
Age in years mean (95% CI)	28.60 (28.56—28.64)	27.55 (27.44—27.67)	28.15 (28.01—28.28)	31.02 (30.83—31.22)	28.74 (28.69—28.78)
Body Mass Index † mean (95% CI)	28.26 (28.21—28.32)	29.79 (29.63—29.95)	28.62 (28.48—28.77)	25.13 (24.94—25.33)	28.09 (28.03—28.15)
Educational status percent (95% CI)					
Did not complete HS or unknown	14.9 (14.6—15.1)	14.6 (13.9—15.3)	31.2 (30.2—32.2)	21.9 (20.4—23.4)	12.1 (11.8—12.4)
Completed HS or GED	30.0 (29.7—30.3)	40.1 (39.1—41.1)	36.3 (35.2—37.3)	18.9 (17.4—20.3)	27.8 (27.4—28.2)
Some college or completed Associate's degree	26.5 (26.2—26.8)	32.3 (31.4—33.2)	21.5 (20.6—22.4)	15.0 (13.6—16.3)	26.8 (26.4—27.1)
Completed Bachelor's degree or higher	28.7 (28.3—29.0)	13.1 (12.4—13.7)	11.1 (10.4—11.7)	44.3 (42.5—46.1)	33.3 (32.9—33.7)

*81 individuals with non-identifiable race and/or ethnicity are included in the All category but not in any race or ethnicity group.

† BMI calculations included the person's self-reported pre-pregnancy weight.

Figure 1



frequency of adverse maternal outcomes in existing literature. Logistic models used to produce aORs were adjusted for the covariates age, BMI and education. In the cases of predicting preterm birth and cesarean section, logistic models were also adjusted for previous preterm birth and previous cesarean section covariates, respectively (Tables 2, 3). In addressing the association between COVID-19 during pregnancy and maternal outcomes, Chi-squared tests of independence were used to produce p-values (Tables 3 – 7). For the cases in which Chi-squared tests were inappropriate due to small cell size, Fisher's exact test was employed (Tables 3 – 7). Unadjusted odds ratios (ORs) as well as aORs were found relative to the non-positive group along with corresponding 95% CIs (Table 3). All analyses were conducted on SAS software version 9.4.

Results

During 2020 in Indiana, there were 76,467 singleton births. Among those giving birth, 1,625 tested positive for COVID-19 during the time of their estimated gestation. This cohort was predominantly White, non-Hispanic, with 72.3% of singleton live births occurring among this group. The remainder of the cohort was Black, non-Hispanic people at 13.3%, Hispanic people of any race at 10.8% and Other, non-Hispanic people at 3.7%. There were 81 individuals who could not be classified within these groups due to unidentifiable race, ethnicity or both. Rates of COVID-19 during pregnancy were significantly higher among Black, non-Hispanic people at 2.53% and Hispanic, any race people at 4.19% as compared to White, non-Hispanic people at 1.74% ($p \leq 0.05$). These rates and corresponding CIs are shown in Figure 1. Notably, the rate among the Hispanic, any race group was significantly higher than that of all other race and ethnicity groups ($p \leq 0.05$).

Table 2: Maternal Outcomes by Race and Ethnicity Among the Non-Positive Group

To establish baseline trends for maternal outcomes by race and ethnicity for this cohort, the non-positive group was analyzed relative to the White, non-Hispanic group. The results are displayed in Table 2. Membership in the Black, non-Hispanic group was a significant risk factor for four out of the ten maternal outcomes investigated. This was more than either of the other groups. It was also, however, a protective factor against two adverse maternal outcomes. Similarly, belonging to the Other, non-Hispanic group was a significant risk factor for two out of the ten outcomes studied and a protective factor against one outcome. In discordance with existing research, however, membership in the Hispanic, any race group was a protective factor against three adverse maternal outcomes and a risk factor for only one outcome.

Table 3: Maternal Outcomes by COVID-19 Status

Table 3 displays positive and non-positive group frequencies of maternal outcomes. Additionally, ORs and aORs relative to the non-positive group are displayed. The COVID-19 during pregnancy group had increased frequencies of all maternal outcomes except for blood transfusions and induced labor. Not all differences between the rates of the two groups,

Table 2: Non-Positive Group Maternal Outcomes by Race and Ethnicity Relative to the Non-Positive White, non -Hispanic Group

Race and Ethnicity Group*	Black, non-Hispanic (n=9869, 13.2%)		Hispanic, any race (n=7918, 10.6%)		Other, non-Hispanic (n=2743, 3.7%)	
	P-value	aOR‡ (95% CI)	P-value	aOR‡ (95% CI)	P-value	aOR‡ (95% CI)
Health Risks†						
Gestational diabetes	**<0.001**	**0.74 (0.68—0.81)**	**<0.001**	**1.39 (1.28—1.52)**	**<0.001**	**2.22 (1.97—2.49)**
Gestational hypertension	0.333	1.04 (0.96—1.11)	**<0.001**	**0.85 (0.78—0.93)**	**<0.001**	**0.66 (0.56—0.78)**
Eclampsia	**0.047**	**1.72 (1.01—2.93)**	0.301	1.42 (0.73—2.75)	0.168	2.07 (0.74—5.79)
Labor and Delivery†						
Abruptio placenta	**<0.001**	**1.66 (1.28—2.15)**	0.064	0.69 (0.47—1.02)	0.316	0.73 (0.40—1.35)
Preterm birth	**<0.001**	**1.41 (1.31—1.51)**	0.148	0.94 (0.86—1.02)	0.455	0.94 (0.81—1.10)
Induction	**<0.001**	**0.83 (0.79—0.87)**	**<0.001**	**0.81 (0.77—0.86)**	0.081	0.93 (0.86—1.01)
Cesarean section	0.238	1.04 (0.98—1.10)	**0.009**	**0.92 (0.86—0.98)**	**<0.001**	**1.25 (1.13—1.38)**
Morbidities†						
ICU admission	**0.003**	**1.94 (1.25—3.01)**	0.883	1.04 (0.59—1.85)	0.265	0.45 (0.11—1.84)
Transfusion	0.076	1.32 (0.97—1.79)	0.249	1.22 (0.87—1.71)	0.171	1.42 (0.86—2.34)
Unplanned OR procedure	0.409	1.17 (0.81—1.69)	0.368	1.20 (0.81—1.77)	0.822	1.08 (0.57—2.05)

*Statistics for all groups are relative to the non-positive White, non-Hispanic group (n=54234, 72.5% of the non-positive group).
† Statistically significant p-values, aORs and 95% CIs are in bold, meeting a threshold of $p \leq 0.05$ after adjustment.
‡All aORs are adjusted for age, BMI and education. For the outcome preterm birth, the aOR is also adjusted for previous preterm birth. For the outcome cesarean section, the aOR is also adjusted for previous cesarean section.

however, proved significant. COVID-19 during pregnancy was significantly associated with increased instances of having gestational diabetes (p = 0.002), giving preterm birth (p= 0.005) and admission to the ICU (p=0.003). The association between COVID-19 and ICU admission was particularly strong. People who were positive had 3.14 (aOR 95% CI: 1.59 - 6.19) times higher odds of admission to the ICU than those who were non-positive. While rates of eclampsia were also significantly higher among the positive group, this significance did not remain after controlling for age, BMI and education.

Tables 4 – 7: Maternal Outcomes by COVID-19 Status within Race and Ethnicity Groups

Much like the results from Table 2, members of the Black, non-Hispanic group proved to have more significant associations than any other race or ethnicity group (Table 4). For those in the Black, non-Hispanic group, positive people were more likely than those who were non-positive to give preterm birth (p = 0.024) and be admitted to the ICU (p = 0.009), even after controlling for age, BMI, education and previous preterm birth. Although positive Black, non-Hispanic people were also more likely to deliver by cesarean section, this increased risk did not remain significant after similar adjustment.

Among members of the Hispanic, any race group (Table 5), COVID-19 during pregnancy associated significantly with having gestational hypertension (p = 0.017) even after adjustment for age, BMI and

Table 3: Maternal Outcomes by COVID-19 Positivity During Pregnancy Status, Whole Cohort

COVID-19 during pregnancy status	Positive* (n=1625, 2.1%)	Non-positive* (n=74842, 97.9%)	P-value	Unadjusted OR (95% CI) relative to Non-positive group	Adjusted OR‡ (95% CI) relative to Non-positive group
Health Risks†					
Gestational diabetes	10.0%	7.9%	**0.002**	**1.30 (1.10—1.53)**	**1.22 (1.03—1.44)**
Gestational hypertension	10.9%	9.7%	0.094	1.14 (0.98—1.34)	1.10 (0.94—1.29)
Eclampsia§	0.3%	0.1%	**0.048**	**2.63 (1.07—6.48)**	2.06 (0.75—5.62)
Labor and Delivery†					
Abruptio placenta	0.7%	0.5%	0.354	1.33 (0.73—2.42)	1.34 (0.73—2.44)
Preterm birth	10.5%	8.5%	**0.005**	**1.26 (1.07—1.48)**	**1.21 (1.03—1.43)**
Induction	39.2%	39.4%	0.856	0.99 (0.90—1.10)	0.98 (0.89—1.09)
Cesarean section	30.2%	28.7%	0.178	1.08 (0.97—1.20)	0.99 (0.87—1.13)
Morbidities†					
ICU admission§	0.6%	0.2%	**0.003**	**3.25 (1.65—6.40)**	**3.14 (1.59—6.19)**
Transfusion	0.5%	0.5%	0.791	1.10 (0.54—2.22)	1.10 (0.54—2.22)
Unplanned OR procedure	0.4%	0.3%	0.486	1.31 (0.62—2.77)	1.32 (0.62—2.80)

*78 individuals are included in the non-positive group, and 3 individuals are included in the Positive group who are not included in Tables 2, 4—7 due to unidentifiable race and/or ethnicity.

†Statistically significant p-values, ORs, aORs and 95% CIs are in bold, meeting a threshold of $p \leq 0.05$.

‡All aORs are adjusted for age, BMI and education. For the outcome preterm birth, the aOR is also adjusted for previous preterm birth. For the outcome cesarean section, the aOR is also adjusted for previous cesarean section.

§P-values for these outcomes are calculated by Fisher's exact test due to small cell size rather than Chi-squared tests, and unadjusted ORs for these outcomes are exact.

education. Given that Hispanic, any race people had a significantly higher rate of positivity than any other race or ethnicity group, it was noteworthy that only one association between COVID-19 and adverse outcomes proved significant.

Unlike the larger cohort and all other race and ethnicity groups, the Other, non-Hispanic cohort (Table 6) had decreased frequencies of adverse maternal outcomes among COVID-19 positive people for most outcomes measured. These associations between COVID-19 and maternal outcomes for members of the Other, non-Hispanic group had the greatest variation from the associations observed in the whole cohort. However, none of the results observed for this group were statistically significant.

Lastly, for members of the White, non-Hispanic group (Table 7), COVID-19 associated significantly with having gestational diabetes when unadjusted for age, BMI and education. As the association did not remain significant after adjustment, a member of the White, non-Hispanic group who is diagnosed with gestational diabetes may find that their diagnosis is better explained by their age, BMI or educational status than COVID-19. Although positive members of this group tended to have higher frequencies of adverse maternal outcomes than non-positive members, none of these associations between COVID-19 and adverse maternal outcomes proved to be significant.

Discussion

During 2020 in Indiana, people who tested positive for COVID-19 during their singleton pregnancy tended to have adverse maternal outcomes more often than those who were non-positive. Among all

singleton births in the state, people who were positive were significantly more likely to have gestational diabetes, give preterm birth and be admitted to the ICU. Within each race and ethnicity group, however, the associations between COVID-19 and maternal outcomes varied. No two groups shared any significant associations. The results suggest that although most groups displayed similar patterns, the Black, non-Hispanic group drove the significance observed in all singleton births for the outcomes of preterm birth and ICU admission. This is because within race and ethnicity groups, the associations between preterm birth, ICU admission and COVID-19 only proved significant for Black, non-Hispanic people. Additionally, within their own ethnicity group, Hispanic, any race people were significantly more likely to have gestational hypertension if they had COVID-19 during pregnancy.

Table 4: Black non-Hispanic Group, Maternal Outcomes by COVID-19 During Pregnancy Status

COVID-19 during pregnancy status	Positive (n=256, 2.5%)	Non-positive (n=9869, 97.5%)	P-value
Health Risks			
Gestational diabetes	9.0%	6.4%	0.093
Gestational hypertension	11.8%	11.0%	0.715
Eclampsia*	0.8%	0.2%	0.106
Labor and Delivery†			
Abruptio placenta*	0.8%	0.8%	1.000
Preterm birth	16.8%	12.1%	**0.024‡**
Induction	39.8%	37.1%	0.365
Cesarean section	38.7%	31.6%	0.016§
Morbidities†			
ICU admission*	1.6%	0.3%	**0.009‡**
Transfusion*	0.4%	0.5%	1.000
Unplanned OR procedure*	0.8%	0.4%	0.240

*P-values for these outcomes are calculated with Fisher's exact test rather than a Chi-squared test due to small cell size.

†Statistically significant p-values are in bold, meeting a threshold of $p \leq 0.05$ after adjustment.

‡Retains significance after adjustment for age, BMI, education and previous preterm birth where appropriate; preterm birth aOR: 1.45 (95% CI: 1.03—2.05); ICU admission aOR: 5.05 (95% CI: 1.76—14.51).

§Does not retain significance after adjustment for age, BMI, education and previous cesarean section; cesarean section aOR: 1.29 (95% CI: 0.95—1.74).

Table 5: Hispanic Any Race Group, Maternal Outcomes by COVID-19 During Pregnancy Status

COVID-19 during pregnancy status	Positive (n=346, 4.2%)	Non-positive (n=7918, 95.8%)	P-value
Health Risks†			
Gestational diabetes	11.6%	10.3%	0.443
Gestational hypertension	11.9%	8.3%	**0.017‡**
Eclampsia*	0.3%	0.1%	0.402
Labor and Delivery			
Abruptio placenta*	0.6%	0.4%	0.375
Preterm birth	9.8%	8.3%	0.310
Induction	35.8%	34.6%	0.642
Cesarean section	24.0%	27.5%	0.155
Morbidities			
ICU admission*	0.3%	0.2%	0.517
Transfusion*	0.9%	0.5%	0.436
Unplanned OR procedure*	1.2%	0.4%	0.068

*P-values for these outcomes are calculated with Fisher's exact test rather than a Chi-squared test due to small cell size.

†Statistically significant p-values are in bold, meeting a threshold of $p \leq 0.05$ after adjustment.

‡Retains significance after adjustment for age, BMI and education; gestational hypertension aOR: 1.48 (95% CI: 1.05—2.08).

Evolving Demographics

Despite White, non-Hispanic people making up the largest share of births, the birthrates from this cohort indicate evolving demographics in the state of Indiana. According to 2020 Census data, Black, non-Hispanic people made up 9.6% of Indiana's population [31], while contributing 13.3% to all singleton live births. Similarly, Hispanic people of any race accounted for 8.2% of the populace [31] and 10.8% of all singleton live births. These birthrates agree with reporting that population growth in Indiana is largely fueled by those who do not identify as White, non-Hispanic [32]. Research with a focus on race and ethnicity groups may prove to be increasingly relevant over time as the U.S. population changes.

Influence of Race and Ethnicity Groups on Whole Cohort Trends

For the whole cohort, the adverse maternal outcomes that associated significantly with COVID-19 were having gestational diabetes, giving preterm birth and admission to the ICU. The association between ICU admission and COVID-19 among pregnant people has been well documented [13 – 16], and the same is true for preterm birth [13, 15, 16]. Gestational diabetes has also been shown to associate with COVID-19, albeit less frequently [14]. Nuances in these trends, however, are revealed by observing this phenomenon in terms of race and ethnicity.

Table 6: Other non-Hispanic Group, Maternal Outcomes by COVID-19 During Pregnancy Status

COVID-19 during pregnancy status	Positive (n=58, 2.1%)	Non-positive (n=2743, 97.9%)	P-value
Health Risks			
Gestational diabetes	12.1%	13.8%	0.712
Gestational hypertension*	3.5%	5.3%	0.768
Eclampsia*	0.0%	0.2%	1.000
Labor and Delivery			
Abruptio placenta*	1.7%	0.4%	0.223
Preterm birth*	12.1%	7.2%	0.192
Induction	31.0%	35.6%	0.468
Cesarean section	29.3%	30.5%	0.848
Morbidities			
ICU admission*	0.0%	0.1%	1.000
Transfusion*	0.0%	0.6%	1.000
Unplanned OR procedure*	0.0%	0.4%	1.000

*P-values for these outcomes are calculated with Fisher's exact test rather than a Chi-squared test due to small cell size.

Preterm Birth and ICU Admission

While all race and ethnicity groups had higher rates of preterm birth among their positive members, this trend was statistically significant only within the Black, non-Hispanic group. Black, non-Hispanic people who had COVID-19 were significantly more likely than their non-positive counterparts to give birth prematurely (p = 0.024, aOR: 1.45, 95% CI: 1.03 - 2.05). As this trend did not meet even liberal measures of significance in any other race or ethnicity groups, this analysis suggests that the rates of premature births among positive Black, non-Hispanic people drove the significance observed for the whole cohort. The same is true for ICU admission. While most other race and ethnicity groups had increased frequencies of ICU admissions among their positive members, the trend was only significant for Black, non-Hispanic people (p = 0.009, aOR: 5.05, 95% CI: 1.76 - 14.51). It is notable that within the White, non-Hispanic group, the association between ICU admission and COVID-19 would have met a more liberal measure of significance (p = 0.062). This analysis suggests, however, that Black, non-Hispanic people with COVID-19 bore the brunt of these two maternal outcomes: preterm birth and ICU admission.

Table 7: White non-Hispanic Group, Maternal Outcomes by COVID-19 During Pregnancy Status

COVID-19 during pregnancy status	Positive (n=962, 1.7%)	Non-positive (n=54234, 98.3%)	P-value
Health Risks			
Gestational diabetes	9.7%	7.6%	0.014†
Gestational hypertension	10.8%	9.9%	0.318
Eclampsia*	0.2%	0.1%	0.247
Labor and Delivery			
Abruptio placenta*	0.6%	0.5%	0.477
Preterm birth	8.9%	7.9%	0.252
Induction	40.8%	40.7%	0.951
Cesarean section	30.3%	28.2%	0.154
Morbidities			
ICU admission*	0.4%	0.2%	0.062
Transfusion*	0.4%	0.4%	0.802
Unplanned OR procedure*	0.1%	0.3%	0.378

*P-values for these outcomes are calculated with Fisher's exact test rather than a Chi-squared test due to small cell size.

†Does not retain significance after adjustment for age, BMI and education; gestational diabetes aOR: 1.23 (95% CI: 0.98—1.53).

Gestational Diabetes

Apart from the Other, non-Hispanic group, all other race and ethnicity groups had increased frequencies of gestational diabetes among people who had COVID-19 during pregnancy. These increased rates, however, were not significantly higher for any race or ethnicity group. It is less clear, then, how race and ethnicity groups contributed to the significant association between COVID-19 and gestational diabetes for all singleton births. While only the White, non-Hispanic group showed a significant association between COVID-19 and having gestational diabetes, that significance did not persist when adjusted for age, BMI and education (aOR: 1.23, 95% CI: 0.98 - 1.53). Obesity, measured by BMI, is a known predictor of being diagnosed with diabetes, and it is also reported by the CDC as a risk factor for severe COVID-19 illness [33]. It was most likely the BMI of members of the White, non-Hispanic group that associated with both their gestational diabetes and their severity of COVID-19 case. Consequently, the severity of their case may have prompted people to get tested and proved positive. It is also noteworthy that Black, non-Hispanic people may be contributing to this whole group trend given that the association between COVID-19 and gestational diabetes within this group would have met more liberal measures of significance ($p = 0.093$). Further research is necessary to determine what factors most strongly associate with developing gestational diabetes.

Compounding Factors for Black, non-Hispanic People

The results of this analysis affirm the immense health challenges associated with being Black in America. Among non-positive people, membership in the Black, non-Hispanic group as compared to White, non-Hispanic was a risk factor for both giving preterm birth ($p < 0.001$, aOR: 1.41, 95% CI: 1.31 - 1.51) and ICU admission ($p = 0.003$, aOR: 1.94, 95% CI: 1.25 - 3.01). Compounding these problems, Black, non-Hispanic people who had COVID-19 during their pregnancies were significantly more likely than even their non-positive counterparts to give preterm birth and be admitted to the ICU. These factors of being Black, non-Hispanic and contracting COVID-19 during a pregnancy put any person at this intersection in a particularly vulnerable place. This analysis suggests that patients, practitioners and policymakers alike should take necessary steps to protect and aid pregnant, Black, non-Hispanic people, especially if that person contracts COVID-19.

Variations in Race and Ethnicity Groups

Rates of gestational hypertension have proved significantly different between pregnant positive and negative groups in existing literature [14, 16], but this outcome was not observed for the whole Indiana 2020 singleton birthing cohort. It was observed, however, for the Hispanic, any race cohort ($p = 0.017$). Among members of the Hispanic, any race group, the odds of having gestational hypertension were 1.48 (aOR 95% CI: 1.05 - 2.08) times higher among positive group members than their non-positive counterparts. Interestingly, within the non-positive group, being Hispanic, any race was a protective factor against being diagnosed with gestational hypertension ($p < 0.001$, aOR: 0.85, 95% CI: 0.78 - 0.93). This implies that without any COVID-19 present, the odds of having gestational hypertension are significantly lower among Hispanic, any race people as compared to White, non-Hispanic people. These two results paint a unique picture of how COVID-19 and gestational hypertension are associated within the Hispanic, any race group: while they have lower odds than White, non-Hispanic people if they are not positive, they have a significantly increased risk within their own ethnicity group if they are positive. As members of this group tested positive for COVID-19 during their pregnancies at a higher rate than all other groups, those who test positive should perhaps monitor their blood pressure more closely for signs of gestational hypertension.

Contrary to the results observed in the rest of the cohort, Other, non-Hispanic people generally had decreased rates of adverse maternal outcomes among positive group members. It remains unclear why this group differed so notably from the rest of the race and ethnicity groups. This could be in part explained by the relatively small sample size of the Other, non-Hispanic group, but there may have

been additional contributing factors to this phenomenon. Further research is needed on associations between COVID-19 and adverse maternal outcomes for Asian, Pacific Islander, Hawaiian Native, American Indian and Alaskan Native people.

Limitations

Several factors may have limited the effectiveness of this analysis. One of these was the nature by which positive people were matched to their birth event data. COVID-19 tests results were stored in NBS, while birth event data was stored by VR. Although people were matched between these two systems on their first name, last name and date of birth, it is possible that there were some cases of false matches. It is also possible that matches were missed, resulting in positive people who were mistakenly categorized as non-positive. Both occurrences, however, should have been relatively rare and should not have had a significant effect on the results.

Another limiting factor in this analysis is the racial and ethnic makeup of the state of Indiana. In the 2020 Census, 77.2% of residents identified as White alone [31]. Consequently, the size of the White, non-Hispanic group dwarfed the size of all other race and ethnicity groups. This could be contributing to the relatively small number of significant results within race and ethnicity groups as compared with the whole cohort. Furthermore, the racial makeup of this birthing cohort was such that Asian, Native American, Alaskan Native, Native Hawaiian and Other Pacific Islander people did not have enough group members to allow for a meaningful analysis when considered separately. Although people in the Other, non-Hispanic group did share their lack of Hispanic ethnicity, their races are certainly distinct from each other. Additional analysis showed that 70.6% of people in the Other, non-Hispanic group were classified as Other Asian or Pacific Islander on the Birth Worksheet (Appendix 1). This majority may have included a high proportion Burmese people, who have a notable presence in Indiana. Burmese populations in Fort Wayne and Indianapolis both rank among the top ten largest in any metropolitan area across the U.S. [34]. The second and third most common classifications among this group were Other Nonwhite at 10.4% and Chinese at 8.8%. Further research on COVID-19 associated maternal outcomes among pregnant people with a focus on race and ethnicity groups should target more diverse populations or combine data across multiple states. This would be important to increase the sample sizes of race groups that were underserved by this analysis.

The nature of COVID-19 testing within this cohort was also a limitation. Not all people who had a singleton birth in Indiana during 2020 were tested for COVID-19. Furthermore, some individuals could have used at-home tests without reporting a positive result at the time of their birth event. Therefore, there are certainly some undiagnosed cases among members of the non-positive group. Depending on the proportion of undiagnosed cases making up the non-positive group, this fact could have masked significant differences in rates of maternal outcomes between the positive and non-positive groups. If the prevalence of COVID-19 testing among pregnant people increases as this pandemic evolves, continued research on this topic should obtain control groups that are entirely negative. While there were people who tested negative during their estimated gestation among the non-positive group in this analysis, there were too few of these people to make up a statistically sound control group. Furthermore, it is possible that members of this cohort who did obtain a COVID-19 test share certain demographic factors that allowed them more ease of access to testing sites. Those who obtained a test would have needed access to reliable transportation, a flexible working schedule and the technology to make an appointment online. Consequently, those who tested positive may be on average more affluent than those who never got tested, and their shared affluence may have had an undetected effect on this analysis. This effect could also be mitigated in future research by a higher prevalence of COVID-19 testing, which would allow for a larger sample of negative people to make up a control group.

The ten outcomes measured may have had confounding factors that were not accounted for in this analysis. An example of one such is the notable

increase in the rates of induced labor during the last three decades [35, 36]. Although this rate has increased for most race and ethnicity groups, it remains the highest among White, non-Hispanic people [35 – 37]. While our purpose was to study the incidence of medical complications among this cohort, the proportion of elective inductions or inductions without any medical indication was unlikely to have been negligible [38, 39]. Without access to indication of induction, it was not possible to exclude those cases. Further research focusing specifically on induced labor and COVID-19 should account for the nature of the induction.

Lastly, it is reasonable that increased rates of elective inductions, as well as other potential confounding factors, may have been exacerbated by the increased stress on pregnant people and medical practitioners alike during the early pandemic phase of 2020. The pandemic-related challenges of staffing shortages and hospital accessibility may have played an unrecognized role in adverse maternal outcomes that was not detected in this analysis. As the pandemic continues, it is of the utmost importance to protect the physical and mental health of pregnant people and medical personnel.

Conclusion

The SARS-CoV-2 virus, more commonly known as COVID-19, is far from eradicated. While we collectively continue to navigate this pandemic, cases that were once incredibly rare – such as a pregnant individual contracting coronavirus – could continue to become more common. People who gave single-ton birth in Indiana during 2020 were significantly more likely to be diagnosed with gestational diabetes, give preterm birth and be admitted to the in-tensive care unit if they had tested positive for COVID-19 during their pregnancy. For two of these outcomes (giving preterm birth and admission to the ICU), the significance observed in the whole co-hort was driven by the strength of the association observed within the Black, non-Hispanic group. Within their own ethnicity group, those who were Hispanic, any race had a significantly increased chance of having gestational hypertension if they had tested positive for COVID-19 during their pregnancy. Given the established association between adverse maternal outcomes and communities of color, alongside the disproportionate effect of COVID-19 on these same communities, this analysis provided a necessary lens through which to observe the association between COVID-19 and maternal outcomes.

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Appendix 1

For each live birth in Indiana, a Certificate of Live Birth Worksheet is completed. A relevant portion of that Birth Worksheet is shown below. These questions on the Birth Worksheet may have been completed by the person who gave birth, filled out by a medical professional under advisement of the person who gave birth or completed by a medical professional from medical records. The process of completing this Live Birth Worksheet likely varied between hospitals and other birthing facilities. This data is then finalized by the National Center for Health Statistics and reported back to Vital Records in the Indiana Department of Health.

Question 22, Certificate of Live Birth Worksheet

22. MOTHER/PARENT: Are you Spanish/Hispanic/Latino? If not Spanish/Hispanic/Latino, check the "No" box. If Spanish/Hispanic/Latino, check the most appropriate box.

- ☐ No, not Spanish/Hispanic/Latino
- ☐ Yes, Mexican, Mexican American, Chicano
- ☐ Yes, Puerto Rican
- ☐ Yes, Cuban
- ☐ Yes, other Spanish/Hispanic/Latino (e.g. Spaniard, Salvadoran, Dominican, Columbian)

(Specify)_____

- ☐ Unknown

Question 23, Certificate of Live Birth Worksheet

23. MOTHER/PARENT: What is your race? (Please check all that apply).

- ☐ White
- ☐ Black or African American
- ☐ American Indian or Alaska Native

(name of enrolled or principal tribe(s)) _____

- ☐ Asian Indian
- ☐ Chinese
- ☐ Filipino
- ☐ Japanese
- ☐ Korean
- ☐ Vietnamese
- ☐ Other Asian

(specify) _____

- ☐ Native Hawaiian
- ☐ Guamanian or Chamorro
- ☐ Samoan
- ☐ Other Pacific Islander

(specify) _____

- ☐ Other

(specify) _____

- ☐ Unknown