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Early coronavirus disease 2019 restrictive measures and changes in maternal characteristics, use of assisted reproductive technology, and stillbirth

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Abstract

Background: The initial COVID-19 pandemic response–related effects on conceptions following the use of assisted reproductive technologies (ART), and on changes in the maternal characteristics of women who conceived during the early vs. pre-pandemic period, have been understudied.

Objectives: To examine the effects of ART clinic closures in the United States (US) in March 2020 on the frequency of ART-conceived live births, multiple births and stillbirths; and to describe changes in the characteristics of women who conceived in the early pandemic period.

Methods: Population-based cohort study including all births in the US from January 2015 to December 2020 (22,907,688 live births; 134,537 stillbirths). Interrupted time series (ITS) methodology was used to estimate rate ratios (RR) of expected versus observed rates in December 2020 (i.e., among births conceived mainly in March 2020).

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Demographic and clinical characteristics were compared between mothers who conceived in March 2020 versus March 2015–2019.

Results: Overall, 1.1% of live births and 1.7% of stillbirths were conceived by ART. ART-conceived live births decreased by 57.0% in December 2020 (observed vs. expected RR 0.43, 95% confidence interval [CI] 0.40, 0.45), and these declines occurred in all subgroups of women. Multiple births also declined in December 2020. Stillbirth rates increased in December 2020 in ART-conceived births (RR 2.55, 95% CI 1.63, 3.92) but remained unchanged in the non-ART group. Maternal characteristics of women who conceived in the early pandemic versus pre-pandemic period differed and included an increased prevalence of pre-pregnancy obesity class 3 and chronic hypertension.

Conclusions: The early pandemic closure of ART clinics resulted in a substantial decline in ART-conceived live births and multiple births in December 2020 and an increase in the proportion of stillbirths among ART-conceived births. Women who conceived in the early pandemic period also had an increased prevalence of obesity and chronic hypertension.

KEYWORDS
assisted reproductive technology, conception, coronavirus disease 2019, multiple birth, pandemic response, stillbirth

1 | BACKGROUND

Although the effects of the COVID-19 pandemic on pregnant women have been extensively evaluated,[1–8] the impact of pandemic response–related measures on rates of live births and stillbirths following conception using assisted reproductive technology (ART) have not received adequate attention. Some of the most impactful measures during the early period of the pandemic included the American Society of Reproductive Medicine ([ASMR] and other scientific and professional fertility societies) guidelines recommending suspension of new fertility treatments.[9–12] A prior study of over 8 million commercially insured women in the United States (US) showed a dramatic decline in ART procedures between February and April 2020 and a subsequent increase, which surpassed the pre-pandemic.[13] This study further showed that changes occurred in all age groups, although lower utilisation rates and slower recovery rates of infertility care were observed among women aged 40 years and older. A survey of US women who were planning or undergoing fertility treatment during the beginning of the pandemic showed a large negative emotional impact of the interruption of the reproductive services, predominantly among women of advanced age and those with diminished ovarian reserve.[14] Similar emotional distress was observed among individuals and couples dealing with infertility in other countries.[15–20] Irrespective of ART use, women may have chosen to postpone conception and childbirth due to pandemic-related uncertainty and financial instability, lack of support from family members due to travel restrictions, and anxiety about the unknown, potentially harmful effects of SARS-CoV-2 infection.[21]

Synopsis

Study question

- To examine the effects of ART clinics closure during the COVID-19 pandemic on rates of ART-conceived live births, multiple births and stillbirths and to describe changes in the characteristics of women who conceived during this period in the United States.

What's already known

- Pandemic-related restrictive measures included closures of ART clinics in March 2020 in the United States and other countries.

What this study adds

- Early pandemic closures of ART clinics resulted in a dramatic reduction in ART-conceived live births in December 2020, a large decline in the proportion of multiple births among all live births, and an increase in stillbirths following ART conception.
- The proportion of women with pre-pregnancy obesity and chronic hypertension increased among those who conceived in March 2020 and had a live birth in 2020.

ART is a risk factor for adverse birth outcomes, primarily due to elevated rates of multiple pregnancy, although the incidence of ART-conceived multiple pregnancies has declined in recent years

after the ASMR's recommendation to increase single-embryo transfer practices.[22–25] Nevertheless, even in a singleton pregnancy, ART is associated with preterm birth, low birth weight, stillbirth at 20–27 weeks gestation and neonatal death.[22]

We examined the effects of ART clinics closures in the US in March 2020 on rates of live births conceived by ART and the frequency of multiple births. First, we examined temporal trends in the proportion of ART-conceived births using birth cohorts (i.e., births that occurred during each month). This analysis was stratified by pregnancy characteristics including maternal age, race/ethnicity, educational status and the type of health care insurance to ascertain if there were disparities in pandemic-related effects among these subpopulations. We also examined changes in the rates of stillbirth following ART conception. Second, we examined temporal trends in ART conception and multiple births in conception cohorts (i.e., births that were conceived during the same period, e.g., in March of each year). A secondary objective of this analysis was to assess whether women in these conception cohorts (conception in the month of March before versus during the pandemic) differed not only in the proportions of ART conceptions and multiple pregnancies but also by other characteristics.

2 | METHODS

2.1 | Study population and data sources

We performed a retrospective cohort study including all live births between 20 and 45 weeks' gestation in the US between January 2015 and December 2020. Data including information from live birth and fetal death certificates from the 50 states and District of Columbia in the US were obtained from the Centers for Disease Control and Prevention (National Center for Health Statistics, NCHS). The NCHS natality and fetal death files include information about maternal demographic and clinical characteristics, maternal age, self-reported height and pre-pregnancy weight, self-reported ART use, maternal comorbidity (e.g., pre-pregnancy diabetes and hypertension), and other clinical data related to childbirth (e.g., gestational age at delivery). Gestational age at delivery was based on obstetric (ultrasound) estimate, and if this was not available, last menstrual period dating was used.

2.2 | Exposure

US birth certificates included self-reported information regarding any treatments that were used to facilitate conception, based on a question with two options worded as follows: "Pregnancy resulted from infertility treatment, if yes, check all that apply (i) Fertility-enhancing drugs, Artificial insemination or Intrauterine insemination; and (ii) Assisted reproductive technology (e.g., in vitro fertilisation [IVF], gamete intrafallopian transfer [GIFT])."[26] ART use was defined as any fertility treatments in which eggs or embryos are handled in the laboratory (such as IVF or intracytoplasmic sperm injection, which is consistent with the CDC definition of ART).[27,28]

We also examined maternal characteristics of women whose estimated month of conception was March 2020, in contrast to women whose estimated month of conception was March 2015 to 2019. For each delivery, gestational age (in completed weeks) was divided by the average number of weeks in a month (4.4), rounded and subtracted from the month of birth to indicate an approximate month of conception (assuming a mid-month conception). Information on births occurring in January 2021 (from the pandemic cohort with estimated conception in March 2020) was not available; we therefore excluded births occurring in January (a few late-term and post-term births) in all comparison conception cohorts to match this exclusion.

2.3 | Outcome

The proportion of ART-conceived live births among all live births in each month between 2015 and 2020 was used to analyse the temporal trends and, in particular, changes occurring in December 2020 as those infants were predominantly conceived in March 2020. We also examined proportions of ART-conceived multiple births among all multiple live births and among all live births to discern the delayed impact of ART clinics closure on ART-conceived births and ART-conceived multiple births. Similarly, we examined rates of stillbirth by calendar month, stratified by mode of conception (ART vs. non-ART).

Secondary outcomes included demographic characteristics of all women with a live birth who conceived in March 2020, as this was the first cohort of women, whose pregnancy was influenced by the COVID-19 pandemic in its entirety. The comparisons were made with respect to age, parity, race/ethnicity, the type of health care insurance, pre-pregnancy body mass Index (BMI) and chronic comorbidity and other characteristics.

2.4 | Statistical analyses

The rates of ART-conceived live births per 1000 live births, ART-conceived multiple live births per 1000 multiple live births, and the rate of multiple live births per 1000 live births were plotted for each month between 2015 to 2020 (birth cohort analyses). We used interrupted time series (ITS) methodology[29] to evaluate a potential reduction in these rates in December 2020, when term infants conceived in March 2020 were expected to be born. Analyses were conducted using segmented Poisson regression models and results were presented graphically and as observed versus expected counts. Interaction terms were included in the model to assess possible modification of the effect of the pandemic on ART births by maternal age, education, race/ethnicity, and the type of health care insurance. This effect modification was

assessed by estimating the relative excess risk due to interaction (RERI) and corresponding 95% confidence intervals, calculated via the delta method.[30] For all models, we calculated the rate difference (RD) and rate ratio (RR) between observed versus expected counts and corresponding 95% confidence intervals (CI). Stillbirth rates were also analysed using ITS, stratified by ART versus non-ART conceptions. CIs for rate differences between observed and expected were calculated by simulating 10,000 draws from a joint normal distribution with means and variances obtained from the Poisson model.[31]

The analyses of conception cohorts included all women who conceived in March (2015–2019 versus 2020) and had a live singleton or multiple birth in December of the same year. Rates of ART conception and other characteristics were contrasted across these cohorts. We used ITS segmented Poisson regression models to discern changes occurring in the pandemic cohort that were above or below the expected based on the temporal trend in the pre-pandemic cohorts. Records with missing values for any covariates (<3.0% in total) were excluded from multivariable analyses (sensitivity analyses were performed for stillbirth rates, see below).

2.5 | Missing data

Missing values for ART treatment in the fetal death files were found predominantly in 2015 and 2016. This was because four US states did not implement the 2003 revision of birth certificates, and data on ART was missing for these states. To determine if this may have biased the trends, we undertook a temporal trend analysis excluding years 2015 and 2016. A few missing values for ART due to non-reporting were also found in the 2015 natality file (<1.8% of live births in 2015), these were excluded form the analyses.

All analyses were carried out using SAS (version 9.4; SAS Institute, Inc., Cary, NC) and R (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Study population and temporal trends

Overall, 22,907,688 live births and 134,537 stillbirths at 20 to 45 weeks' gestation occurred in the US between 2015 and 2020. We excluded 68,972 live births (0.3 per 1000 live births) and 3123 stillbirths (23 per 1000 stillbirths) from the main analysis due to missing information on ART conception, yielding a total of 22,838,716 live births and 131,414 stillbirths. The proportions of ART-conceived births were 1.1% ($n = 256,764$) among live births and 1.7% ($n = 2171$) among stillbirths.

Rates of ART-conceived live births by month are shown in Figure 1A and Table S1. There was a seasonal variation in ART rates, characterised by a sharp decline in the month of September of each year. Nevertheless, rates of ART-conceived live births showed a progressively increasing temporal trend from 2015 onwards. However, this rising rate fell abruptly in December 2020 and the fall substantially exceeded the decline typically seen in September (e.g., the number of ART-conceived live births was 1789 in December 2020 compared with 4259 such births in December 2019, Table S1). The ITS model showed an estimated 57.0% decline in ART live births in December 2020 (RR 0.43, 95% CI 0.40, 0.45). The decline in ART live births occurred in all categories of maternal age, race/ethnicity, education and insurance status, although the magnitude of the decrease varied; the degree of decline differed by maternal age and the type of health care insurance (Table 1), with largest decline in women aged ≥35 years.

Temporal trends in rates of ART-conceived live births among all multiple live births were characterised by a steady decline, seasonal drops in September, and a sharp decline in November and December in 2020 (Figure 1B). The proportion of multiple live births among all live births also dropped in November 2020 and then further declined sharply in December 2020 (corresponding to a decline in ART-conceived births in March 2020 and consequent reductions in preterm and term live births in November and December 2020; Figure 1C).

The rates of stillbirth were relatively unchanged in the non-ART group. However, in the ART group, stillbirth rates declined between January 2015 and October 2019 and then increased in December 2020 (Figure 2). The corresponding rate ratios between observed and expected rates of stillbirths were 1.06 (95% CI 1.00, 1.12) versus 2.55 (95% CI 1.63, 3.92), respectively (see Table S1 for the frequency and rates of stillbirth).

3.2 | Secondary analyses

The pandemic conception cohort (estimated conception in March 2020 with a live birth in 2020) included 281,909 mothers, while the conception month-matched comparison cohorts (estimated conception in March 2015–2019) included 1,543,876 mothers (Table 2). The rate of ART conception was lower in the pandemic cohort; the adjusted RR was 0.49 (95% CI 0.47, 0.52). Compared with the expected maternal characteristics based on the pre-pandemic temporal trend, women who conceived in March 2020 were less likely to have used ART and fertility drugs and were less likely to have had a multiple birth. The proportions of women who were ≥35 years, Asian, and uninsured (self-pay or health care insurance other than Medicaid and private) declined. We observed larger than expected proportions of women with pre-pregnancy obesity class 3 and those with chronic hypertension, the proportion of women with chronic hypertension was 8.0% higher than expected based on the temporal trend prior to the pandemic; Table 2. The proportion of out-of-hospital births in the pandemic cohort increased by 27.0% above expected (Table 2).

The rate ratios between observed and expected rates of stillbirths were similar to the primary analysis after excluding years

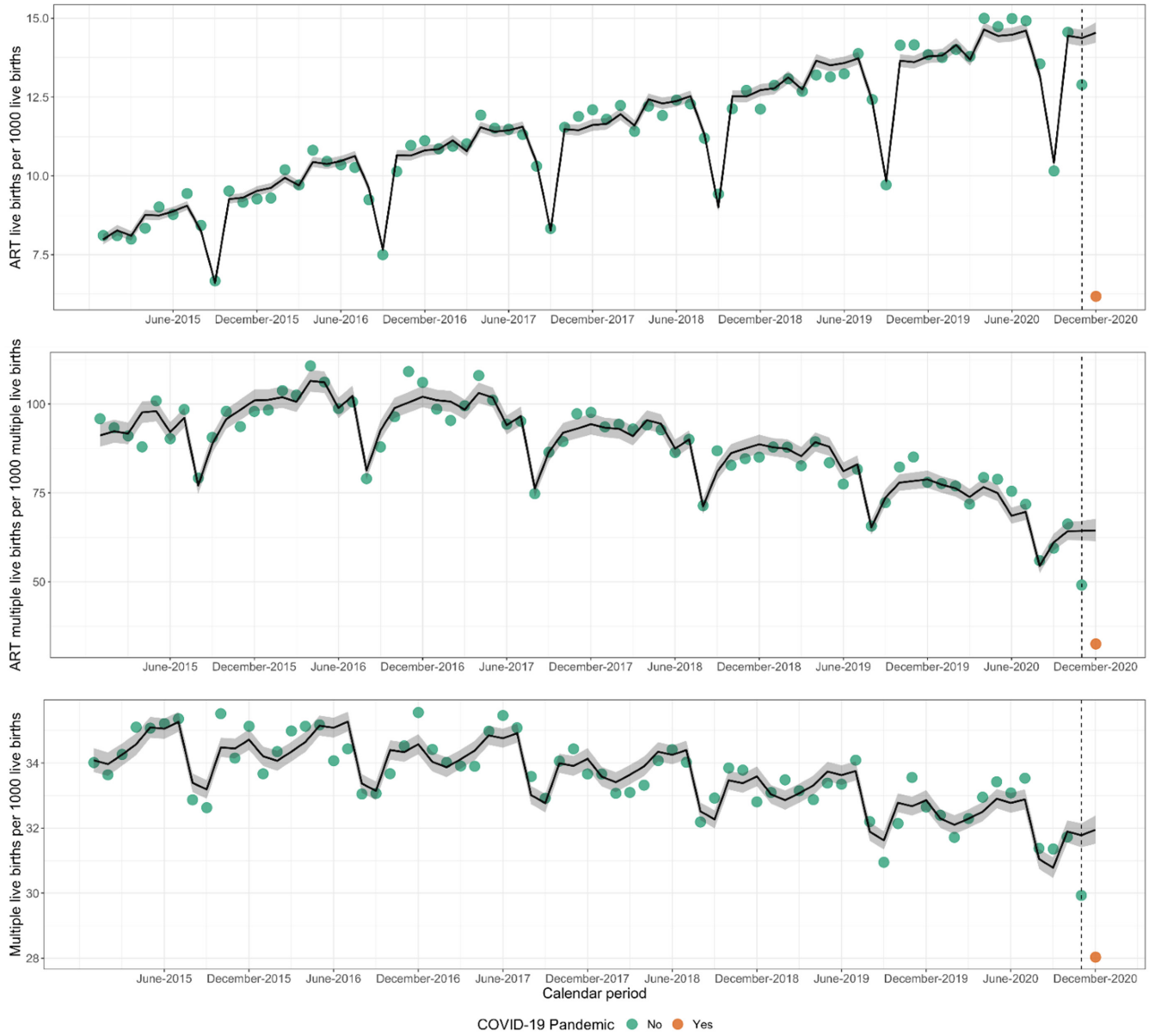

FIGURE 1 Live births conceived following the use of assisted reproductive technology (ART) as a proportion of all live births (A); ART-conceived multiple live births as a proportion of all multiple live births (B); and the proportion of multiple live births among all live births (C) by month; the Unites States, 2015–2020. Green dots: pre-pandemic conception; Orange dot: pandemic conception; gray-shaded zones represent confidence intervals.

2015 and 2016; RR 1.08 (95% CI 1.01, 1.16) in non-ART group and RR 2.26 (95% CI 1.43, 3.58) in ART group.

4 | COMMENT

4.1 | Principal findings

This study shows a delayed pandemic effect on reproductive health, highlighted by a dramatic drop in the number of ART-conceived live births and a lower proportion of multiple live births in the last month(s) in 2020. The large declines in ART-conceived live births and in multiple live births follow pandemic-induced ART clinics closures in March 2020. Our study also documents the delayed effects of annual (holiday-related) ART clinics closures in late December and early January that manifest as declines in ART-conceived births in the following September. Temporal trends in stillbirth rates showed an increase in stillbirths among women with ART-conception in December 2020 among women who conceived with ART and this corresponds to conception which occurred in March 2020. Additionally, the exploratory analyses show changes in some maternal characteristics among women whose estimated conception was in the first month of the pandemic, including increases in the prevalence of obesity class 3 and chronic hypertension, and a decline in the proportion of Asian mothers, mothers ≥35 years, and those without health care insurance.

TABLE 1 Expected versus observed rates of ART-conceived infants (per 1000 live births) in December 2020, stratified by maternal characteristics

Maternal characteristics	Expected rate per 1000 live births *N* = 4213	Observed rate per 1000 live births *N* = 1791	Rate difference per 1000 live births (95% CI)	Rate ratio (95% CI)	RERI (95% CI)[a]
Overall	14.6	6.2	−8.4 (−8.0, −8.7)	0.43 (0.40, 0.45)	–
Health care insurance					
Medicaid	1.9	1	−0.9 (−0.8, −1.00)	0.54 (0.44, 0.64)	0.0 (Reference)
Private	26.8	11.3	−15.5 (−14.9, −16.1)	0.42 (0.40, 0.45)	−11.5 (−12.7, -10.4)
Self-pay	5.1	2.6	−2.5 (−1.9, −3.1)	0.51 (0.35, 0.75)	−1.5 (−2.3, −0.6)
Other	11.6	3.7	−7.9 (−6.8, −9.1)	0.32 (0.23, 0.45)	−3.9 (−4.8, −3.0)
Age (years)					
<25	0.5	0.4	−0.1 (0.0, −0.2)	0.72 (0.47, 1.10)	−10.4 (−12.4, −8.4)
25–34	9.8	4.6	−5.2 (−5.0, −5.5)	0.47 (0.43, 0.50)	0.0 (Reference)
≥35	44.9	18.7	−26.2 (−25.1, −27.4)	0.42 (0.39, 0.44)	−50.2 (−59.0, −41.3)
Race/ethnicity					
Non-Hispanic White	18.2	7.9	−10.3 (−9.9, −10.8)	0.43 (0.41, 0.46)	0.0 (Reference)
Non-Hispanic Black	5.4	2.8	−2.6 (−2.2, −3.0)	0.52 (0.43, 0.62)	0.4 (0.4, 0.5)
AIAN	3.6	1.8	−1.8 (−0.7, −3.6)	0.49 (0.17, 1.40)	0.5 (0.3, 0.6)
Asian	33.8	13.8	−20.0 (−18.6, −21.6)	0.41 (0.36, 0.47)	−0.6 (−0.7, −0.4)
Hispanic	5.5	2.7	−2.8 (−2.4, −3.1)	0.50 (0.42, 0.58)	0.4 (0.3, 0.5)
Education					
Less than high school	1.2	0.7	−0.5 (−0.3, −0.7)	0.60 (0.39, 0.91)	0.5 (0.5, 0.6)
High school or higher	16.3	6.9	−9.4 (−9.1, −9.8)	0.42 (0.40, 0.45)	0.0 (Reference)

Abbreviations: AIAN, American Indian or Alaska Native; ART, assisted reproductive technologies; CI, confidence interval.

[a]RERI denotes relative excess risk due to interaction.

4.2 | Strengths of the study

Strengths of our study include its population-based character and the consistent data collection across the study period. NCHS data include out-of-hospital births, which limits selection bias, as the proportion of these births increased during the pandemic.[32] ITS analyses accounted for seasonal variation and temporal trends occurring prior to the pandemic. We also used two types of analyses, namely, birth cohort and conception cohort analyses, which showed almost identical results.

4.3 | Limitations of the data

Our study has several limitations. First, the frequency of ART conception may have been underestimated due to self-reporting.[33] However, this underestimation is likely to have been consistent across the study period, and this would have minimised the bias in our finding regarding a relative decline in ART rates. Even though the degree of underestimation of ART conception may differ in groups of women with various demographic characterises, whose prevalence may have changed over time, our analyses stratified by several key characteristics showed similar declines. Second, our estimates of the month of conception were calculated using month of birth and gestational age (in weeks) and are therefore somewhat imprecise (i.e., some women in our pandemic cohort may have conceived by ART in late February or early March prior to ART clinics closure). This misclassification may have led to an underestimation of the temporal changes occurring in the pandemic-exposed cohort. Third, data on live births in the US in 2021 were not available (when the study was finalised); limiting the time frame of our study to changes during the initial weeks of the pandemic. Zhou et al.[13] showed that the recovery in the use of fertility services was quite rapid in a large sample of commercially insured women in the US, suggesting that the decline in the rate of live births following ART was limited to 2–3 months. Fourth, we lacked data on miscarriage which precluded an assessment of changes in the rate of fetal loss before 20 weeks' gestation (the conception cohorts in our study were reconstructed from birth cohorts and are therefore incomplete and left-truncated). Further studies should elucidate the temporal trends in miscarriage and stillbirth in ART-conceived pregnancies and monitor trends beyond 2020.

4.4 | Interpretation

The early months of the COVID-19 pandemic had unprecedented effects on health care delivery and utilisation, limiting the treatments

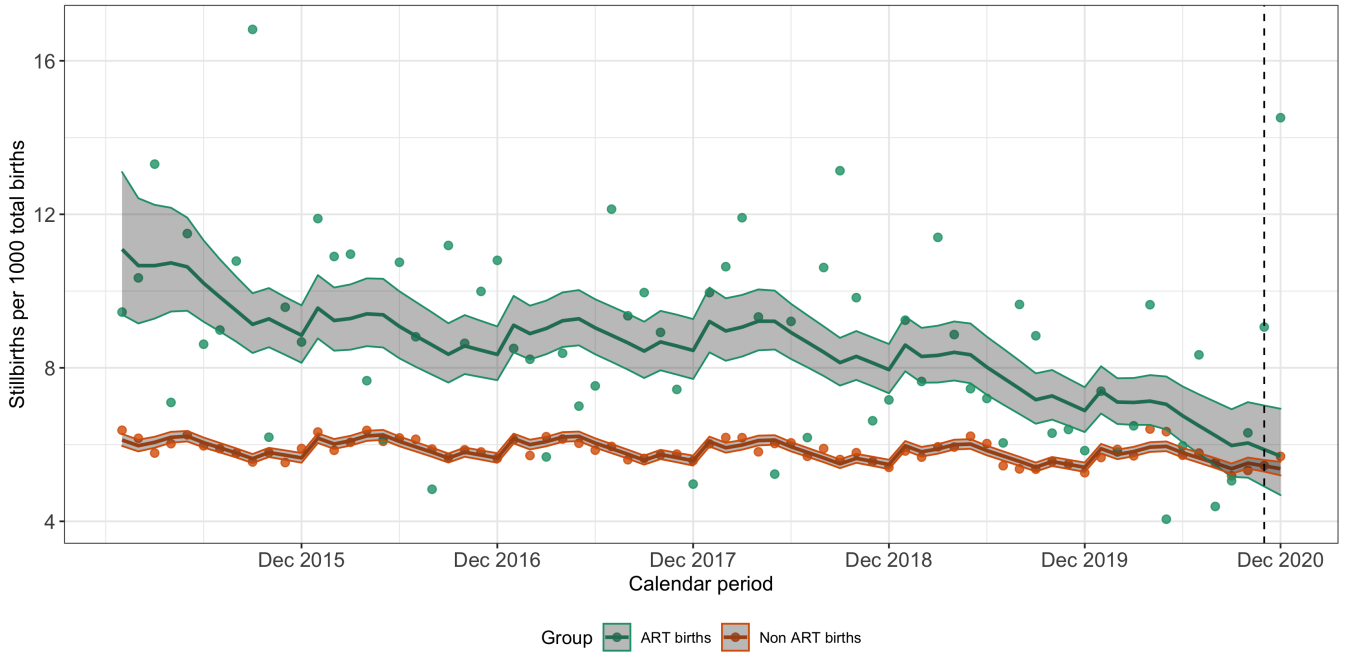

FIGURE 2 Monthly rates of stillbirth per 1000 total births stratified by ART conception; the Unites States, 2015–2020. Gray-shaded zones represent confidence intervals; dots represent rates; dashed horizontal line represents Match 2020.

of acute and chronic medical conditions. While time-sensitive, the treatment of infertility is generally not considered urgent.[34] In March 2020, the ASRM recommended suspending the initiation of new fertility treatment cycles.[29,34] It is difficult to estimate what proportion of ART clinics followed the ASRM guidelines as compliance is not compulsory. A survey of US women showed that only 12.7% of women (or couples) had continued with their infertility treatment during the early pandemic.[14] It is possible that women who continued the ART treatment may have had specific conditions that contributed to the urgency to proceed with the treatment, but also increased the risk of stillbirth (e.g., advanced age). It is also possible that the limited post-conception follow-up visits and access to obstetric services contributed to the increased risk of stillbirth among these women. We have focused predominantly on temporal changes in the month of December; however, the temporal decline in ART-conceived births is apparent also in November 2020, which is likely due to a decline in ART-conceived pregnancies in March 2020 that resulted in preterm birth.

Besides the dramatic drop in ART births observed in December 2020, smaller declines in the rate of ART-conceived live births are also evident in September of previous years as a delayed effects of ART clinics holiday closures. Such consistency of delayed effects is congruous with causal associations. However, in contrast to planned closures occurring in December every year, the unplanned abrupt cessation of fertility treatments in the early pandemic had negative effects on affected women and their partners with respect to their reproductive choices and mental health. The ART clinics resumed their services in April 2020, which may have led to a compensatory increase in ART-conceived births and in multiple pregnancies. Our results are consistent with a prior study[35] that also showed an 86.6% drop in ART-conceived births in December 2020 in the Lombardy region in Italy.

Infertility and ART are associated with an increased risk of adverse pregnancy outcomes including early pregnancy loss, preterm birth, small-for-gestational-age live birth, stillbirth, and neonatal death.[23,25,36,37] The available data from the COVID-19 pandemic show that SARS-CoV-2 infection by itself is not associated with an increased risk of early pregnancy loss or stillbirth.[38–40] A study from Germany[41] including 1485 women with SARS-CoV-2 infection found higher rates of preterm birth and NICU admission among women with medically assisted conception in the early pandemic compared with women with spontaneous conception; however, the elevated risks were due to non-ART-related risk factors, which is also consistent with our results.

There is a need for national guidelines establishing measures that fertility clinics should take to prepare for future pandemics, as the emotional toll on individuals and couples with infertility is significant,[14–20] and delays in fertility treatment can lower the success rate in older women and those with diminished ovarian reserve. On the other hand, the characteristics of the pandemic-causing pathogen are typically unknown in the early pandemic period and potential risks to pregnant women and their offspring have to be balanced with the risks associated with the delay in fertility treatments.

In general, the changes in characteristics of women who conceived (spontaneously or by ART) during this period were small with respect to differences in the proportions of risk factors for adverse outcomes, except for an increase in the prevalence of pre-pregnancy obesity and chronic hypertension. The latter increased 8.0% above the expected value estimated based on the already increasing temporal trend prior to the pandemic.

TABLE 2 Changes in demographic and clinical characteristics of mothers with singleton or multiple live births and estimated conception in March before the COVID-19 pandemic (2015–2019) vs. early in the pandemic (March 2020)

Maternal characteristics	2015 *N* = 320,958	2016 *N* = 313,985	2017 *N* = 307,248	2018 *N* = 302,515	2019 *N* = 299,170	2020 *N* = 281,909	Rate Ratio[a] (95% CI)
ART conception	2458 (0.8)	2980 (1.0)	3238 (1.1)	3302 (1.1)	3862 (1.3)	2009 (0.7)	0.49 (0.47, 0.52)
ART multiple pregnancy	513 (0.2)	557 (0.2)	510 (0.2)	426 (0.1)	425 (0.1)	180 (0.1)	0.47 (0.39, 0.55)
Medically assisted non-ART conception[b]	2081 (0.7)	2309 (0.7)	2303 (0.8)	2285 (0.8)	2249 (0.8)	1487 (0.5)	0.66 (0.62, 0.70)
Multiple pregnancy (all)	5377 (1.7)	5335 (1.7)	5302 (1.7)	5130 (1.7)	5027 (1.7)	4104 (1.5)	0.86 (0.82, 0.89)
Maternal age (years)							
<25	88,603 (27.6)	82,106 (26.1)	77,698 (25.3)	73,789 (24.4)	71,756 (24.0)	67,365 (23.9)	1.04 (1.03, 1.06)
25–34	179,319 (55.9)	177,492 (56.5)	174,455 (56.8)	172,865 (57.1)	170,285 (56.9)	162,349 (57.6)	1.00 (1.00, 1.01)
≥35	53,036 (16.5)	54,387 (17.3)	55,095 (17.9)	55,861 (18.5)	57,129 (19.1)	52,195 (18.5)	0.93 (0.92, 0.94)
Race/ethnicity							
Non-Hispanic White	163,987 (51.5)	157,509 (50.6)	154,622 (50.8)	151,243 (50.4)	147,517 (49.8)	140,860 (50.4)	1.02 (1.01, 1.03)
Non-Hispanic Black	47,875 (15.0)	47,144 (15.2)	46,676 (15.3)	45,784 (15.3)	46,076 (15.5)	43,455 (15.6)	1.00 (0.98, 1.01)
AIAN	2629 (0.8)	2522 (0.81)	2345 (0.8)	2335 (0.8)	2272 (0.8)	2116 (0.8)	1.02 (0.96, 1.08)
Non-Hispanic Asian	19,952 (6.3)	21,475 (6.9)	20,231 (6.6)	19,659 (6.6)	19,712 (6.6)	16,187 (5.8)	0.86 (0.84, 0.88)
HNOPI	778 (0.2)	786 (0.2)	802 (0.3)	789 (0.3)	843 (0.3)	826 (0.3)	1.02 (0.92, 1.13)
Non-Hispanic other	6724 (2.1)	6550 (2.1)	6779 (2.2)	6815 (2.3)	6810 (2.3)	6828 (2.4)	1.03 (1.00, 1.07)
Hispanic	76,455 (24.0)	75,067 (24.1)	73,183 (24.0)	73,182 (24.4)	73,044 (24.6)	69,038 (24.7)	1.00 (0.99, 1.01)
Low maternal education	46,208 (14.6)	43,556 (14.1)	40,602 (13.4)	38,780 (13.0)	37,023 (12.6)	33,495 (12.1)	1.00 (0.99, 1.01)
No prenatal care[c]	4893 (1.6)	5061 (1.7)	5339 (1.8)	5580 (1.9)	5458 (1.9)	5465 (2.0)	0.98 (0.95, 1.02)
Smoking during pregnancy	24,575 (7.7)	22,248 (7.1)	21,028 (6.8)	19,555 (6.5)	17,557 (5.9)	15,810 (5.6)	1.00 (0.98, 1.02)
Out-of-hospital birth	4569 (1.4)	4620 (1.5)	4611 (1.5)	4681 (1.6)	4442 (1.5)	5527 (2.0)	1.27 (1.22, 1.32)
Health care insurance							
Medicaid	140,778 (44.2)	137,507 (44.1)	134,327 (44.0)	130,392 (43.4)	129,398 (43.5)	123,136 (44.0)	1.02 (1.01, 1.02)
Private	151,972 (47.7)	149,376 (47.9)	146,764 (48.0)	145,991 (48.6)	145,241 (48.9)	136,607 (48.8)	0.99 (0.98, 1.00)
Self-pay	13,106 (4.1)	13,281 (4.3)	12,756 (4.2)	12,903 (4.3)	12,248 (4.1)	10,595 (3.8)	0.90 (0.87, 0.92)
Other	12,903 (4.0)	11,899 (3.8)	11,655 (3.8)	11,304 (3.8)	10,258 (3.4)	9723 (3.5)	0.95 (0.93, 0.97)
Primipara	124,802 (39.0)	122,070 (39.0)	119,374 (38.9)	117,578 (39.0)	117,315 (39.3)	111,943 (39.8)	1.02 (1.01, 1.02)
Body mass index							
Underweight	11,012 (3.5)	10,697 (3.5)	10,149 (3.4)	9311 (3.1)	8757 (3.0)	7846 (2.8)	0.98 (0.95, 1.01)
Normal BMI	137,754 (44.2)	133,380 (43.7)	127,152 (42.4)	121,946 (41.2)	117,910 (40.3)	107,692 (38.9)	0.99 (0.98, 1.00)
Overweight	80,838 (25.9)	79,588 (26.1)	78,843 (26.3)	79,072 (26.7)	78,542 (26.8)	74,740 (27.0)	1.00 (0.99, 1.01)

TABLE 2 (Continued)

Maternal characteristics	2015 N = 320,958	2016 N = 313,985	2017 N = 307,248	2018 N = 302,515	2019 N = 299,170	2020 N = 281,909	Rate Ratio[a] (95% CI)
Obesity class 1	44,646 (14.3)	44,484 (14.6)	45,141 (15.1)	45,560 (15.4)	46,476 (15.9)	45,300 (16.4)	1.01 (0.99, 1.02)
Obesity class 2	21,736 (7.0)	21,552 (7.1)	22,216 (7.4)	23,021 (7.8)	23,577 (8.1)	23,551 (8.5)	1.02 (1.00, 1.04)
Obesity class 3	15,578 (5.0)	15,627 (5.1)	16,134 (5.4)	16,790 (5.7)	17,251 (5.9)	17,654 (6.4)	1.04 (1.01, 1.06)
Pre-pregnancy diabetes	2724 (0.9)	2820 (0.9)	2899 (0.9)	3008 (1.0)	3047 (1.0)	3164 (1.1)	1.04 (0.99, 1.09)
Chronic hypertension	5265 (1.6)	5652 (1.8)	6067 (2.0)	6289 (2.1)	6842 (2.3)	7527 (2.7)	1.08 (1.04, 1.12)

Abbreviations: AIAN, American Indian or Alaskan Native; ART, assisted reproductive technology; CI, confidence interval; NHOPI, Native Hawaiian or Other Pacific Islander.

[a]Rate ratio expressing the ratio of observed proportion versus ITS estimated expected proportion of women.

[b]Fertility treatment except those in which eggs or embryos are handled in the laboratory.

4.5 | Conclusions

This study highlights the delayed effects resulting from the early COVID-19 pandemic and related response measures, specifically changes in ART-conceived live births and maternal characteristics. ART conceptions declined dramatically in the early period of the pandemic, and this has implications especially for women of advanced reproductive age, women with reduced ovarian reserve and those in need for cryopreservation due to higher risks of infertility owing to cancer treatments. Further analyses are warranted to document how these trends evolved during the latter stages of the pandemic, including temporal changes in stillbirth rates and other adverse pregnancy outcomes, and to examine the underlying causes of the pandemic-related changes.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

SL drafted the article, JNB and SL conducted the analyses. All authors made substantial contributions to the conception and design of the study, interpretation of findings, revising the manuscript critically for important intellectual content, and approving the final version as submitted.

DATA AVAILABILITY STATEMENT

All data used in this study are publicly available in deidentified form at https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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