Impact of the COVID-19 Pandemic on Excess Perinatal Mortality and Morbidity in Israel

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Abstract

Objective The 2020 COVID-19 pandemic has been associated with excess mortality and morbidity in adults and teenagers over 14 years of age, but there is still limited evidence on the direct and indirect impact of the pandemic on pregnancy. We aimed to evaluate the effect of the first wave of the COVID-19 pandemic on obstetrical emergency attendance in a low-risk population and the corresponding perinatal outcomes.

Study Design This is a single center retrospective cohort study of all singleton births between February 21 and April 30. Prenatal emergency labor ward admission numbers and obstetric outcomes during the peak of the first COVID-19 pandemic of 2020 in Israel were compared with the combined corresponding periods for the years 2017 to 2019.

Results During the 2020 COVID-19 pandemic, the mean number of prenatal emergency labor ward admissions was lower, both by daily count and per woman, in comparison to the combined matching periods in 2017, 2018, and 2019 (48.6 ± 12.2 vs. 57.8 ± 14.4, $p < 0.0001$ and 1.74 ± 1.1 vs. 1.92 ± 1.2, $p < 0.0001$, respectively). A significantly ($p = 0.0370$) higher rate of stillbirth was noted in the study group (0.4%) compared with the control group (0.1%). All study group patients were negative for COVID-19. Gestational age at delivery, rates of premature delivery at <28, 34, and 37 weeks, pregnancy complications, postdate delivery at >40 and 41 weeks, mode of delivery, and numbers of emergency cesarean deliveries were similar in both groups. There was no difference in the intrapartum fetal death rate between the groups.

Conclusion The COVID-19 pandemic stay-at-home policy combined with patient fear of contracting the disease in hospital could explain the associated higher rate of stillbirth. This collateral perinatal damage follows a decreased in prenatal emergency labor ward admissions during the first wave of COVID-19 in Israel.

Keywords
- COVID-19
- pandemic
- IUFD
- SARS-COV-2
- stillbirth

Key Points

- Less obstetrical ER attendance is observed during the pandemic.
- There is a parallel increase in stillbirth rate.
- Stillbirth cases tested negative for COVID-19.
- Lockdown and pandemic panic are possible causes.

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Excess deaths due to coronavirus disease 2019 (COVID-19), following the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China in late December 2019 is now well documented. Pooled estimates of all-cause mortality for 24 European countries/federal states, participating in the European monitoring of excess mortality for public health action network for the period March to April 2020, have shown excess mortality in all age groups over 14 years old.[1] In Israel, the first COVID-19 case was diagnosed on February 21, 2020, and from the beginning of March onward, strict restrictions on movement and gathering were imposed. On March 11, 2020, COVID-19 was declared a pandemic by the World Health Organization (WHO)[2] and on March 23, 2020, full lockdown was imposed in Israel.

The importance of routine obstetrical care is well established, especially in high-risk pregnancies, and health authorities around the world have issued instructions and guidance for antenatal and perinatal care not to be disrupted during the COVID-19 pandemic. The identification of pregnant women needing rapid interventions, including induction of labor or emergency cesarean section, is considered as critical as interventions for cardiovascular emergencies.[3–6] Furthermore, even if most pregnant women infected with COVID-19, only develop mild or moderate symptoms,[7–10] early reports published in April and May 2020 showed that women in the third-trimester of gestation were at higher risk for critical illness[7] and preterm cesarean delivery for maternal indications.[10–12]

Recent studies have shown that most neonates born to infected mothers are asymptomatic, and there is only limited evidence suggesting vertical transmission.[7,8,11,13] A small case series of five stillbirths in infected mother from Brazil has suggested that secondary chorioamnionitis due to COVID-19 as the cause for fetal death.[14] A population-based descriptive study using the UK Obstetric Surveillance System has reported a 2.5-fold increase in incidence of stillbirth at the beginning of the pandemic compared with the national rate in 2019.[15] A more recent study from one center in the United Kingdom comparing the changes in incidence of stillbirth and preterm birth has also found an increase in stillbirths between February 1 and mid-June 2020 compared with October 1, 2019 and January 31, 2020.[16] However, as there is a seasonal impact on births and stillbirths,[17,18] the comparison of different periods of the year may have skewed the data in both studies.

For a short period of time, at the start of the pandemic, access to antenatal clinics was limited due to the need for maternity services to put in place special measures required to prevent nosocomial transmission of COVID-19 and medical staff shortage due to self-isolation after exposure to an infected patient or relative. In addition, and similarly to other medical specialities such as cardiovascular diseases,[3–6] pregnant women's fear of contracting infection during a hospital visit must have had an impact on prenatal consultation attendance. In the present study, we have evaluated the effect of the first peak of the COVID-19 pandemic in Israel on prenatal care and obstetrical outcomes compared with the same periods for the year 2017, 2018, and 2019.

Materials and Methods

This is a retrospective cohort study of prenatal care and obstetrical outcomes between February 21 and April 30, 2020, compared with the same period of the year in 2017, 2018, and 2019.

Study Population

All pregnant women with singleton gestation admitted during the COVID-19 peak period (study group) and the corresponding period in 2017 to 2019 (control group) to the labor ward in Shamir Medical Center (Zerifin, Israel), which is a tertiary and university-affiliated hospital, with approximately 9,000 deliveries per a year were included in the study. Premature previable deliveries <24 weeks, multiple pregnancies, and deliveries following feticide were excluded from the study groups. Demographic, obstetrical, and neonatal data were retrieved from computerized medical records and the hospital's laboratory database. Data collected for each participant included maternal age, gravidity, parity, and previous cesarean deliveries. Obstetrical and neonatal data collected included, induction of labor, mode of delivery and indication for cesarean delivery if preformed, date and time of birth, Apgar's score at 5 minutes, arterial umbilical cord pH, neonatal intensive care unit (NICU) admission, and perinatal mortality. For stillbirth cases, stillbirth-weight percentiles were calculated according to nationally accepted growth curves for gestational week and gender.[19] In addition, the following were reviewed: maternal COVID-19 test results at admission, presence of meconium stained or bloody amniotic fluid at the time of membrane rupture, pregnancy follow-up, placental and umbilical cord abnormalities as examined by the department of pathology, and fetal dysmorphism as noted in the labor ward following obstetric and midwife examination after delivery.

The primary outcome was fetal death, categorized into antepartum (stillbirth) or intrapartum. Secondary outcomes were gestational age at birth, maternal diabetes, maternal pregnancy induced hypertension, induction of labor, mode of delivery, type of cesarean delivery (elective, nonelective, or intrapartum), birthweight, 5-minute Apgar's score, umbilical artery cord pH, and NICU admission (for more information, please refer to "Definitions" in the ►Supplementary Material, available in the online version).

The study was approved by the local institutional review board (approval no. 0134–20-ASF). Informed consent was waived due to the retrospective design of the study.

Statistical Analysis

The SAS (SAS Cooperation, Version 34.0, NC) data analysis and statistical software package was used to analyze the data. A standard Kurtosis analysis indicated that the values were normally distributed, and the data are therefore continuous variables presented as mean and standard deviation. Categorical variables are presented as count and percentages. Pearson's Chi-square test or Fisher's exact test, as appropriate, were used to compare between the study and control groups with respect to categorical variables. Independent samples *t*-test was used to compare the means of the two groups for continuous variables. All *p*-values were determined with two-tailed tests. A *p*-value of <0.05 was considered statistically significant.

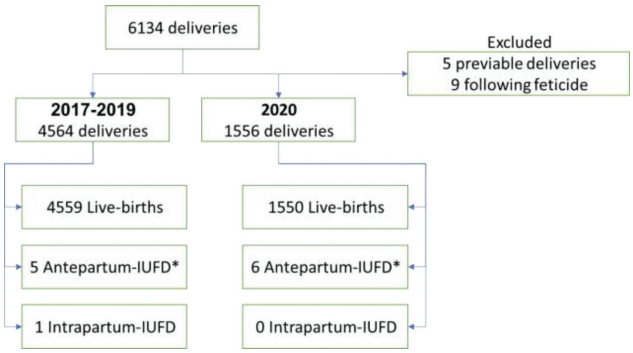

Fig. 1 Study flowchart. *$p = 0.0370$.

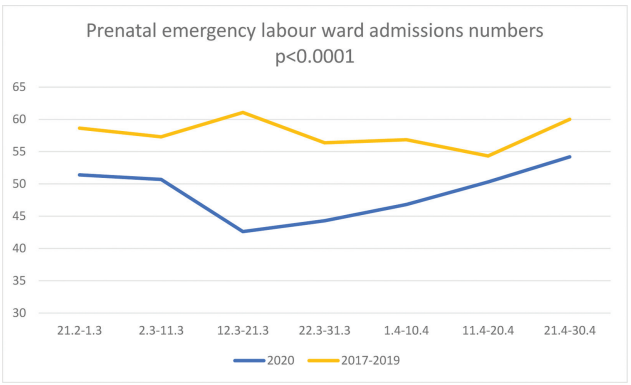

Fig. 2 Prenatal emergency labor ward admissions; $p < 0.0001$. For graphical purposes, data are presented in 10 days average.

Results

There were 1,556 births registered during first wave of the COVID-19 pandemic. The control group included 1,578, 1,545, and 1,441 newborns that were delivered during the same period of the year in 2017, 2018, and 2019, respectively (►Fig. 1).

Maternal age, race/ethnicity, the rate of prior cesarean deliveries, maternal diabetes, and hypertensive rates were all similar between groups (►Table 1). The mean gravidity and parity were increased in the study group (3.0 ± 2.0 vs. 2.7 ± 1.7, $p < 0.0001$; 1.5 ± 1.6 vs. 1.3 ± 1.3, $p < .0001$; gravidity and parity, for the study and control groups, respectively), and the nulliparity rate did not differ between groups (30.2 vs. 32.2%, $p = 0.15$).

During the 2020 COVID-19 pandemic, the average number of prenatal emergency labor ward admission was lower, both by daily count and per woman, in comparison to the combined corresponding periods in 2017 to 2019 (48.6 ± 12.2 vs. 57.8 ± 14.4, $p < 0.0001$; 1.74 ± 1.1 vs. 1.92 ± 1.2, $p < 0.0001$, respectively; ►Fig. 2).

A significantly ($p = 0.037$) higher rate of stillbirth was found in the study group (6/1,556, 0.4%) compared with the control group (5/4,564, 0.1%). There was no difference in the mean gestational age at the diagnosis of fetal death or the postdelivery stillbirth mean weight between study and control groups (35.7 ± 5.2 vs. 36.2 ± 5.0, $p = 0.90$; $2,074 \pm 987$ g vs. $2,633 \pm 1,066$ g, $p = 0.43$; gestational weeks at fetal death diagnosis and stillbirth weight, study, and control groups, respectively). Women in both groups self-referred for medical evaluation after either experiencing decreased fetal movements or contractions. A stillbirth was diagnosed in the absence of fetal heartbeat on ultrasound examination. Women were delivered either vaginally or by cesarean section depending on obstetrical indication. All the women who experienced stillbirth in the study group were tested and found negative for COVID-19.

In five out of the total 11 cases of stillbirth recorded in the study and control groups, histopathology findings were suggestive of placental insufficiency. In three of these cases in the study group, the fetal birthweight was below the 10th centile for gestational age, whereas in the controls one stillbirth presented with anhydramnios and one presented with both a birth weight below the 10th centile and anhydramnios. Histopathologic findings suggesting a cord accident as the cause of fetal death were found only in the study group including one case with a true knot of cord and the other with a pathological narrowing of a portion of the cord. One stillbirth from each group presented with blood in the amniotic fluid, suggesting a placental abruption. One stillbirth in the study group was diagnosed with chorioamnionitis due to

Table 1 Baseline demographic and clinical characteristics of study and control groups

Characteristic		Study group 2020 ($n = 1,556$)	Control group 2017–2019 ($n = 4,564$)	*p*-Value
Age (mean ± SD), y		30.8 ± 5.4	30.5 ± 5.3	0.1963
Gravidity (mean ± SD)		3.0 ± 2.0	2.7 ± 1.7	<0.0001
Parity (mean ± SD)		1.5 ± 1.6	1.3 ± 1.3	<0.0001
Number of nulliparous (*n*, %)		470 (30.2)	1,468 (32.2)	0.1484
≥1 previous cesarean delivery (*n*, %)		186 (12.0)	532 (11.7)	0.7510
Maternal diabetes (*n*, %)		109 (7.0)	371 (8.1)	0.1551
Maternal hypertension disorder (*n*, %)		49 (3.1)	181 (4.0)	0.1439
Ethnicity	Mother was born in Africa or east Asia	91 (5.8)	334 (7.3)	0.0967
	Mother was born elsewhere	1,465 (94.2)	4,226 (92.7)	

Abbreviation: SD, standard deviation.

Table 2 Antepartum and intrapartum fetal death and associated factors in study and control groups

Outcome	Study group 2020 ($n = 1,556$)	Control group 2017–2019 ($n = 4,564$)	*p*-Value
Stillbirth (*n*, %)	6 (0.4)	5 (0.1)	0.0370
Gestational age at fetal death diagnosis (wk, mean ± SD)	35.7 ± 5.2	36.2 ± 5.0	0.8969
Stillbirth weight (g, mean ± SD)	2,074 ± 987	2,633 ± 1,066	0.4338
Stillbirth small for gestational age (n, %)	3/6 (50%)	1/5 (20%)	0.5455
Anhydramnios (*n*, %)	0/6 (0%)	2/5 (40%)	0.1818
Cord finding suggest potential cord accident (*n*, %)	2/6 (33%)	0/5 (0%)	0.4545
Blood stained amniotic fluid (*n*, %)	1/6 (17%)	1/5 (20%)	1.0
Meconium stain amniotic fluid (*n*, %)	1/6 (17%)	2/5 (40%)	0.5455
Chorioamnionitis (*n*, %)	1/6 (17%)	0/5 (0%)	1.0
Intrapartum intrauterine fetal death (*n*, %)	0 (0.0%)	1 (0.03%)	0.4804

Abbreviations: *n*, number; SD, standard deviation.

Table 3 Perinatal Outcomes for study and control groups

Outcome		Study group 2020 ($n = 1,556$)	Control group 2017–2019 ($n = 4,564$)	*p*-Value
Gestational age at birth (wk, mean ± SD)		39.32 ± 1.7	39.28 ± 1.7	0.4296
Premature delivery < 28 gestational weeks (*n*, %)		5 (0.3)	11 (0.2)	0.5922
Premature delivery < 34 gestational weeks (*n*, %)		17 (1.1)	51 (1.1)	0.9355
Premature delivery < 37 gestational weeks (*n*, %)		82 (5.3)	278 (6.1)	0.2345
Postdate delivery > 40 gestational weeks (*n*, %)		530 (34.1)	1,538 (33.7)	0.7937
Postdate delivery > 41 gestational weeks (*n*, %)		135 (8.7)	346 (7.6)	0.1658
Induction of labor (*n*, %)		502 (32.3)	1,258 (28.2)	0.0005
Mode of delivery	Spontaneous vaginal delivery (*n*, %)	1,184 (76.1)	3,473 (76.1)	0.9656
	Vacuum-assisted vaginal delivery (*n*, %)	99 (6.4)	283 (6.2)	
	Cesarean delivery (*n*, %)	273 (17.5)	809 (17.7)	
Type of cesarean delivery	Elective (*n*, %)	91 (33.2)	255 (31.5)	0.8225
	Nonelective (*n*, %)	54 (19.7)	156 (19.3)	
	Nonelective, intrapartum (*n*, %)	129 (47.1)	398 (49.2)	
Birthweight (g, mean ± SD)		3,230 ± 490	3,206 ± 477	0.0986
5-minute Apgar's score < 7 (*n*, %)		11 (0.7)	13 (0.3)	0.0214
Umbilical artery pH < 7.1 (*n*, %)		2 (0.9)	32 (2.6)	0.1068
NICU admission (*n*, %)		57 (3.7)	212 (4.7)	0.1464

Abbreviations: *n*, number; NICU, neonatal intensive cate unit; SD, standard deviation.

Escherichia coli. One case from the study group and two from the control group presented with meconium stained amniotic fluid. Two women from the control group had no pathological findings. Two women from the study group had a previous stillbirth. All stillbirth infants were examined in detailed by the perinatal pathologist, and none showed dysmorphic signs. None of the women who experienced stillbirth had diabetes or hypertension.

One case of intrapartum fetal death occurred in the control group, but none were reported in the study group (►Table 2). Gestational age at birth and rates of premature delivery at <28, 34, and 37 weeks, postdate delivery at >40 and 41 weeks, mode of delivery, and number of emergency cesarean delivery were similar in both groups. The induction of labor rate in the study group was higher compared with the control group (32.3 vs. 28.2% of all deliveries, study, and control group respectively, $p = 0.0005$). The study group had more cases of 5-minute Apgar's score lower than 7 (0.7 vs. 0.3%, $p = 0.021$), but the umbilical artery pH and the NICU admission rates did not differ (►Table 3).

Principal Findings of the Study

The data of our study indicate that the first wave of the COVID-19 pandemic was associated with a decline in pregnant women

attendance to the obstetrical emergency room, which could explain a parallel increase in the stillbirth rate compared with the same period in the previous 3 years. As all stillbirth cases in the present study tested negative for COVID-19 virus, the higher stillbirth rate may be considered as collateral damage from the stay at home mandates and fear of catching the virus in the hospital setting during the early stage of the pandemic.

Comparison with Existing Literature

The COVID-19 pandemic has placed tremendous strain on health care systems worldwide across all medical specialities. From the start of the outbreak, many health care workers from different medical emergency specialities noticed a reduction in patient admissions for diseases not directly related to SARS-CoV-2 infections. In particular, a decline in the number of hospital admissions for acute coronary syndrome has been observed across Italy and United States during the peak of the COVID-19 pandemic, which correlates with higher mortality and morbidity.[3–6] A similar reduction in pediatric emergency department attendance with delayed treatment was also observed in Italy in March 2020 compared with previous years, resulting in poorer outcomes in many cases.[20]

By contrast to countries such as Italy, Spain, China, and the United States, the number of hospitalized patients with COVID-19 in Israel was relatively low and did not impact on the distribution of emergency medical services for non-COVID-19 related conditions.[21] Most health care resources were not relocated to manage the COVID-19 pandemic, and in particular, there were no competing needs for equipment and lack of beds in our hospital. Our data therefore suggest that the decrease in prenatal emergency labor ward admission in our study was mainly due to the fear by pregnant women of contracting SARS-CoV-2. This fear was particularly high after the media diffused the news that the infection was largely spread across hospitalized patients and health care personnel due to the lack of personal protection equipment. This patient factor has been reported in previous pandemics[9] and may lead to pregnant women ignoring symptoms such as decreased fetal movements or not getting standard obstetrical care including regular glycemic control or screening for hypertensive disorders, which are known to be associated with higher stillbirth rate.[22,23]

Clinical Implications

Most women infected with COVID-19 are asymptomatic and national survey of the outcome of 427 pregnant women admitted to hospital with confirmed SARS-CoV-2 infection between March 1, 2020 and April 14, 2020 has found that 10% required intensive care support and 1% died.[15] SARS-CoV-2, outcomes are linked to various preexisting comorbidities such as hypertension or diabetes and morbidity disproportionately, affects those of lower socioeconomic status and particularly ethnic minorities.[24]

The recent study by Khalil et al[16] found fewer nulliparous women and showed both a decrease in the number of pregnant women with hypertension and an increase in the number of stillbirths at the start of the pandemic compared with the period immediately before. Our data confirm an increase in stillbirths at the peak of the COVID-19 pandemic in Israel, that is, February 21 and April 30, 2020 compared the same periods of 3 consecutive years before accounting for the seasonal[17,18] effect. By contrast, we found no differences in maternal hypertension and nulliparity rates between the groups. We also observed no difference in the premature delivery rates for any gestational periods at between 28 and 37 weeks, indicating that the increase in stillbirth rate was the main perinatal impact of the of the COVID-19 pandemic in Israel.

None of the women with pregnancies complicated by stillbirth included in the present study tested positive for COVID-19. Women from ethnic minorities account for less than 10% in our population, which is much lower that the United States[16] or the United States. Although the rates of stillbirths increased significantly during the peak of the COVID-19 pandemic in our population, it remains overall much lower than in the United States. These findings suggest that complications such as diabetes and hypertension, which are more common in women from ethnic minorities, did not influence the stillbirth rate in our study. Other confounding factors including as reduced mobility and exercise, increase smoking exposure, increased caloric intake, poor glycemic control for pregestational and gestational diabetic women, poor supervision, and control of hypertensive complications, as well as uncontrolled thyroid disorders[23,25] could have indirectly contributed to risk of stillbirth during the lockdown.

Strengths and Limitations

The strengths of our study lie in it being from a single center, with uniform data documentation and clinical evaluation approach. In addition, to the best of our knowledge, this is the first study investigating the association between obstetrical care during the COVID-19 pandemic and stillbirth. The main limitation of our study is its retrospective design, with limited data available for some parameters. In addition, multiple gestations, which are a major risk factor for stillbirth, were excluded because of their relatively small number in this short period. Because of religious reasons, the Israeli population often declines postmortem autopsies, and therefore, this information is limited to placental examination in both the study and control groups. However, all cases of stillbirth are examined externally by a trained perinatal pathologist and did not show evidence of fetal dysmorphism in both groups. A considerable reduction in the community clinic activity could have influenced the availability of medical services, but these data were not available.

Conclusion

The COVID-19 pandemic is a generation-defining global medical phenomenon, the scope, scale, and pace of which is unprecedented. Despite the limited impact of SARS-CoV-2 on the overall health of pregnant women, our data have shown a decrease in prenatal emergency labor ward admissions parallel with an increase in the number of stillbirths during the first peak of the COVID-19 pandemic. This collateral damage was not due to a reduce access to our maternity

services during that period but is more likely due to the patient fear of contracting the infection during hospital visits, and like for other medical specialities may have discouraged them to access emergency medical services during the first peak of the COVID-19 pandemic. These findings support government guidance in maintaining adequate emergency prenatal care during pandemic and in informing pregnant women about the need to attend routine prenatal consultation.

Conflict of Interest

None declared.

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