



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

A marked decrease in preterm deliveries during the coronavirus disease 2019 pandemic



OBJECTIVE: Previous studies comparing the coronavirus disease 2019 pandemic period with prepandemic periods reported either no change or a decrease in extremely preterm birth (PTB) rates during the pandemic.^{1,2} These studies evaluated a limited number of potential PTB confounders and a short pandemic period. We aimed to determine the change in the PTB rate and neonatal outcomes during the pandemic period compared with that in the prepandemic periods by evaluating multiple obstetrical characteristics during more than 3 pandemic months.

STUDY DESIGN: We compared maternal, obstetrical, and neonatal outcomes of singleton pregnancies at the Sheba Medical Center, Israel, during 3 periods: from March 20, 2020 (date of implementation of governmental state of lockdown), to June 27, 2020 (group 1); a parallel period in 2019 (group 2); and parallel annual periods in 2011–2019 (group 3) (Table 1). We also compared maternal and pregnancy characteristics during the pandemic and corresponding prepandemic periods in 2019 between pregnancies complicated by PTB at <34 0/7 and ≥34 0/7 weeks' gestation (Table 2). Multivariate

TABLE 1

Comparison of maternal, obstetrical, and delivery characteristics and neonatal outcomes between the pandemic (March 2020 to June 2020) and prepandemic periods (from March 2019 to June 2019)

Characteristic	COVID-19 period (n = 2594)	Prepandemic period (2019; n = 2742)	OR (95% CI) ^a	P value	Prepandemic-matched period (2011–2019; n = 28,686)	OR (95% CI) ^a	P value
Maternal characteristics							
Age, y	32.00±5.40	32.00±5.10	—	.329	32.00±5.10	—	.018
Prepregnancy BMI, kg/m ²	23.50±4.60	23.60±4.70	—	.285	23.30±4.40	—	.011
Predelivery BMI, kg/m ²	28.20±4.50	28.40±4.50	—	.119	28.20±4.40	—	.381
Weight gain, kg	13.00±5.40	13.00±5.90	—	.190	13.00±5.50	—	<.001
Immigrant	387 (14.90)	440 (16.00)	—	.257	4772 (16.60)	0.88 (0.79–0.99)	.024
Smoking	107 (4.10)	117 (4.30)	—	.796	1386 (4.80)	—	.106
Parity	1.00±1.50	1.00±1.60	—	.584	1.00±1.40	—	.001
Nulliparous	877 (33.80)	952 (34.70)	—	.484	10,271 (35.80)	0.92 (0.85–0.99)	.042
Previous cesarean delivery	425 (16.40)	457 (16.70)	—	.781	4551 (15.90)	—	.489
Positive SARS-CoV-2 ^b test	13	—	—	—	—	—	—
Assisted reproductive technology	221 (8.50)	238 (8.70)	—	.835	2082 (7.30)	1.19 (1.03–1.39)	.018
Diabetes	297 (11.40)	285 (10.40)	—	.216	2615 (9.10)	1.28 (1.14–1.47)	<.001
Hypertensive disease	117 (4.50)	125 (4.60)	—	.932	1118 (3.90)	—	.125
Hemoglobin before delivery, g/dL	12.19±1.10	11.98±1.10	—	<.001	11.92±1.10	—	<.001
Hemoglobin of <11.0 g/dL before delivery	357 (13.80)	5289 (18.40)	0.87 (0.63–0.79)	<.001	503 (18.30)	0.71 (0.61–0.82)	<.001
Platelets before delivery, K/μL	201.00±57.20	211.00±59.90	—	<.001	205.00±57.10	—	<.001
White blood cell count before delivery, K/μL	10.90±3.00	11.10±3.30	—	.264	11.40±3.20	—	<.001

Meyer. Preterm deliveries during the coronavirus disease pandemic. *Am J Obstet Gynecol* 2021.

(continued)

TABLE 1

Comparison of maternal, obstetrical, and delivery characteristics and neonatal outcomes between the pandemic (March 2020 to June 2020) and prepandemic periods (from March 2019 to June 2019) (continued)

Characteristic	COVID-19 period (n = 2594)	Prepandemic period (2019; n = 2742)	OR (95% CI) ^a	P value	Prepandemic-matched period (2011–2019; n = 28,686)	OR (95% CI) ^a	P value
Fibrinogen before delivery, mg/dL	474.00±100.90	468.00±96.90	—	.298	446.00±84.90	—	<.001
Delivery characteristics							
Induction of labor	295 (11.40)	286 (10.40)	—	.270	2793 (9.70)	1.19 (1.05–1.35)	.007
Intrapartum fever	35 (1.30)	30 (1.10)	—	.396	281 (1.00)	—	.071
Gestational age at delivery, wk	39 1/7±1 6/7	39 0/7±2 0/7	—	.004	39 1/7±2 1/7	—	.684
<37 0/7	174 (6.70)	220 (8.00)	—	.066	2060 (7.20)	—	.370
<34 0/7	32 (1.20)	74 (2.70)	0.45 (0.30–0.68)	<.001	592 (2.10)	0.60 (0.41–0.85)	.004
<32 0/7	20 (0.80)	45 (1.60)	0.47 (0.27–0.79)	.004	379 (1.30)	0.58 (0.37–0.92)	.017
Spontaneous delivery	1746 (67.30)	1812 (66.10)	—	.352	19,961 (69.60)	0.90 (0.82–0.98)	.014
Operative vaginal delivery	187 (7.20)	197 (7.20)	—	.972	1735 (6.00)	1.22 (1.04–1.43)	.018
Cesarean delivery	661 (25.50)	733 (26.70)	—	.299	6990 (24.40)	—	.206
Intrapartum cesarean delivery	277 (41.90)	325 (44.30)	—	.366	3083 (44.10)	—	0.276
Neonatal outcomes							
Birthweight, g	3230±511	3196±544	—	.020	3205±533	—	.026
Composite neonatal outcome ^c	118 (4.50)	163 (5.90)	0.76 (0.59–0.96)	.023	1530 (5.30)	—	.087
Stillbirth	22 (0.80)	22 (0.80)	—	.853	290 (1.00)	—	.424
Death in 30 d	3 (0.10)	4 (0.10)	—	1.0	23 (0.10)	—	.427
Mechanical ventilation	24 (0.90)	23 (0.80)	—	.736	271 (0.90)	—	.922
Hypoxic-ischemic encephalopathy	2 (0.10)	2 (0.10)	—	1.0	27 (0.10)	—	1.0
Convulsions	1 (0.01)	5 (0.20)	—	.220	25 (0.10)	—	.720
Asphyxia	0 (0.00)	1 (0.01)	—	1.0	32 (0.10)	—	.108
1-min Apgar score of <5	9 (0.30)	13 (0.50)	—	.469	193 (0.70)	0.51 (0.26–1.01)	.060
5-min Apgar score of <7	8 (0.30)	8 (0.30)	—	.911	113 (0.40)	—	.502
Neonatal intensive care unit admission	78 (3.00)	123 (4.50)	0.66 (0.50–0.88)	.005	1048 (3.70)	—	.091

Data are presented as mean±standard deviation or number (percentage).

OR was calculated only for significantly different categorical variables.

Apgar, appearance, pulse, grimace, activity, and respiration; BMI, body mass index; CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^a Prepandemic data were compared with COVID-19 period data; ^b SARS-CoV-2 infection was evaluated only during the COVID-19 pandemic. During the study period, only women from endemic areas or women with symptoms of COVID-19 were screened for infection; ^c Composite neonatal outcome consisted of any of the following: stillbirth, neonatal death during the first 30 days, mechanical ventilation, hypoxic-ischemic encephalopathy, convulsions, asphyxia, 1-minute Apgar score of <5, 5-minute Apgar of <7, and neonatal intensive care unit admission.

Meyer. Preterm deliveries during the coronavirus disease pandemic. *Am J Obstet Gynecol* 2021.

TABLE 2

Comparison of maternal, obstetrical, and delivery characteristics and neonatal outcomes between pregnancies complicated by PTB at <34 0/7 and ≥34 0/7 weeks' gestation during the pandemic (March 2020 to June 2020) and prepandemic periods (from March 2019 to June 2019)

Characteristic	Delivery at <34 0/7 wk (n=106)	Delivery at ≥34 0/7 wk (n=5230)	OR (95% CI)	P value	aOR (95% CI) ^a	P value
Age, y	32.00±7.30	32.00±5.40	—	.430	—	—
Prepregnancy BMI, kg/m ²	23.10±3.90	23.60±4.60	—	.396	—	—
Predelivery BMI, kg/m ²	26.20±4.50	28.40±4.50	—	<.001 ^b	—	—
Weight gain, kg	9.00±3.60	13.00±5.70	—	<.001 ^b	0.93 (0.90–0.97) ^c	<.001 ^b
Immigrant	13 (12.3)	814 (15.6)	—	.353	—	—
Smoking	8 (7.5)	216 (4.1)	—	.082	—	—
COVID-19 period	32 (30.2)	2562 (49.0)	0.45 (0.29–0.68)	<.001 ^b	0.29 (0.15–0.56)	.001 ^b
Parity	1.00±1.60	1.00±1.50	—	.509	—	—
Nulliparous	45 (42.5)	1784 (34.1)	—	.073	—	—
Previous cesarean delivery	23 (21.7)	859 (16.4)	—	.148	—	—
Assisted reproductive technology	21 (19.8)	438 (8.4)	2.70 (1.66–4.40)	<.001 ^b	3.57 (1.92–6.61)	<.001 ^b
Diabetes	11 (10.4)	571 (10.9)	—	.860	—	—
Hypertensive disease	8 (7.5)	234 (4.5)	—	.132	—	—
Hemoglobin before delivery, g/dL	11.23±2.20	12.10±1.10	—	<.001 ^b	—	—
Hemoglobin of <11 g/dL before delivery	33 (31.1)	827 (15.8)	2.40 (1.58–3.65)	<.001 ^b	2.89 (1.64–5.10)	<.001 ^b
Induction of labor	26 (24.5)	555 (10.6)	2.73 (1.74–4.29)	<.001 ^b	3.41 (1.90–6.43)	<.001 ^b
Intrapartum fever	2 (1.9)	63 (1.2)	—	.372	—	—

Data are presented as mean±standard deviation or number (percentage).

aOR, adjusted odds ratio; BMI, body mass index; COVID-19, coronavirus disease 2019; OR, odds ratio; PTB, preterm birth.

^a aOR following multivariate regression analysis include the following factors: weight gain, COVID-19 period, assisted reproductive technology, hemoglobin before delivery, and induction of labor;

^b P<.05; ^c For every kg increase in weight gain.

Meyer. Preterm deliveries during the coronavirus disease pandemic. *Am J Obstet Gynecol* 2021.

regression analysis was performed to study independent factors associated with PTB. The institutional review board approved this study (7068-20-SMC; March 30, 2020).

RESULTS: There were 2594 deliveries during the pandemic period (group 1) and 2742 and 28,686 deliveries in the prepandemic periods (groups 2 and 3, respectively). Maternal and obstetrical characteristics did not differ between groups 1 and 2. Predelivery hemoglobin levels were higher in the pandemic period. PTB rate at <34 0/7 weeks' gestation was significantly lower in the pandemic period than in the parallel period (group 2) (odds ratio [OR], 0.45; 95% confidence interval [CI], 0.30–0.68; P<.001), as was the rate of composite neonatal outcome (OR, 0.76; 95% CI, 0.59–0.96; P=.023). Age, body mass index, parity, diabetes rates, and hematologic characteristics differed between groups 1 and 3 with significantly higher predelivery hemoglobin levels in group 1. PTB rate at <34 0/7 weeks'

gestation was lower in the pandemic period (OR, 0.60; 95% CI, 0.41–0.85; P=.004). On multivariate regression analysis, childbirth during the pandemic period was independently associated with a decreased risk of delivery at <34 0/7 weeks' gestation (adjusted OR, 0.29; 95% CI, 0.15–0.56; P=.001).

CONCLUSION: We observed more than 50% reduction in the rate of PTB at <34 0/7 weeks' gestation, possibly resulting in improved neonatal outcomes.

Explanations for the lower PTB rate include reduced iatrogenic PTBs, avoidance of infections, or reduced stress level related to the lockdown policy. Another suggested etiology is heme oxygenase-1 (HO-1) induction, caused by relative hypoxia resulting from wearing a face mask during the pandemic period. HO-1 enhances hemoglobin production and has been shown to reduce spontaneous PTB rates.^{3,4} However, the clinical significance of hemoglobin level differences is questionable.

Although a Danish study reported lower rates of PTB at ≤ 27 6/7 weeks' gestation during the pandemic, it evaluated only 1 month of the pandemic period and was based on a national registry.¹ Another study has found a trend ($P=.07$) toward higher PTB rates during the pandemic.² However, the sample size was limited, and the prepandemic period comparison was not parallel, potentially introducing seasonal effects.⁵

Further research is required to better understand the pathogenesis underlying lower PTB rates during the pandemic period. ■

Raanan Meyer, MD
Yossi Bart, MD
Abraham Tsur, MD
Yoav Yinon, MD
Department of Obstetrics and Gynecology
Chaim Sheba Medical Center
Tel Hashomer 52621
Ramat Gan, Tel Aviv, Israel
Sackler Faculty of Medicine
Tel Aviv University
Tel Aviv, Israel
raananmeir@gmail.com

Lior Friedrich, BSc
Nitzan Maixner, BSc
Faculty of Health Sciences
Joyce and Irving Goldman Medical School

Ben-Gurion University of the Negev
Beer-Sheva, Israel

Gabriel Levin, MD
Department of Obstetrics and Gynecology
Hadassah-Hebrew University Medical Center
Jerusalem, Israel

The authors report no conflict of interest.

The source of this research is the Chaim Sheba Medical Center, Ramat Gan, Israel.

REFERENCES

1. Hedermann G, Hedley PL, Bækvad-Hansen M, et al. Danish premature birth rates during the COVID-19 lockdown. *Arch Dis Child Fetal Neonatal Ed* 2020. [Epub ahead of print].
2. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA* 2020;324:705–6.
3. Neubauer JA, Sunderram J. Heme oxygenase-1 and chronic hypoxia. *Respir Physiol Neurobiol* 2012;184:178–85.
4. Tsur A, Kalish F, Burgess J, et al. Pravastatin improves fetal survival in mice with a partial deficiency of heme oxygenase-1. *Placenta* 2019;75:1–8.
5. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of air pollution and heat exposure with preterm birth, low birth weight, and stillbirth in the US: a systematic review. *JAMA Netw Open* 2020;3:e208243.

© 2020 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2020.10.017>

Enhanced recovery after cesarean: impact on postoperative opioid use and length of stay



OBJECTIVE: Enhanced recovery after surgery (ERAS) refers to a comprehensive program to improve surgical outcomes.¹ ERAS typically includes preoperative health optimization, preoperative patient education, and perioperative interventions to reduce pain, nausea, vomiting, infection, thromboembolism, and overall morbidity. The ERAS Society recently published guidelines for enhanced recovery after cesarean (ERAC).² ERAC may reduce postoperative opioid use³ and shorten length of stay (LOS),⁴ although these benefits are not always obtained.⁵ The purpose of this quality improvement project was to develop, implement, and evaluate an ERAC program at our level 3 community hospital. Several specific goals were prospectively stated: to reduce postoperative opioid use, to promote earlier removal of bladder catheters (a surrogate for mobilization), and to shorten postoperative LOS.

STUDY DESIGN: Preexisting unit standards (applied routinely for virtually all cesarean deliveries) included some typical ERAS components, such as preoperative prophylactic cefazolin, early postoperative feeding, and routine postoperative use of abdominal binder. A bundle of new

interventions was phased in from August 2018 to November 2018, as summarized in the [Figure](#). Some interventions became new unit standards: allowing clear liquids until 2 hours before surgery, povidone-iodine vaginal cleansing, intraoperative underpatient warming, postoperative chewing gum to prevent nausea, and a new anesthesia preoperative order set that included routine famotidine and acetaminophen plus optional antiemetics and gabapentin. For patients undergoing spinal anesthesia, the dose of intrathecal morphine was standardized to 150 mcg. A new ERAC postoperative order set was used at individual obstetricians' discretion. It included prophylactic ketorolac, ibuprofen, and acetaminophen given around the clock; early removal of bladder catheter; and prophylactic antiemetic medications. ERAC patients were offered an optional 30-minute one-on-one teaching session 1 to 3 days preoperatively and a carbohydrate-loading drink (50 g maltodextrin and fructose in 300 cc) 3 to 4 hours preoperatively (except patients with diabetes). The ERAC order set was available for all cesarean deliveries whether or not the patient had a scheduled procedure, preoperative