BRIEF COMMUNICATION

Low Covid-19 infection rate period is associated with a rebound increase in preterm birth rate

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OBJECTIVE

Several studies have reported lower rates of preterm births (PTB) during the Covid-19 pandemic, while others have not shown this association [1]. These publications have studied the pandemic period in comparison to pre-pandemic periods. In Israel, following a significant reduction in new Covid-19 infections, averaging a weekly 4.3:100,000 new cases, the last lockdown was concluded on April 20, 2021 [2]. This remarkably low infection rate lasted through June 30, 2021. Considering the contradicting reports on PTB rates during the Covid-19 pandemic, and to evaluate the effect of infection burden on obstetrical outcomes, we aimed to study preterm births (PTB)s rate during this low Covid-19 infection rate period (LIRP) and compare it to the pre-pandemic period and a high infection rate period (HIRP).

STUDY DESIGN

A retrospective cohort study from a tertiary medical center, including all deliveries at ≥ 24 weeks gestation. We compared outcomes between three periods: 19/03/2019-19/03/2020 (pre-pandemic period which parallels the following HIRP), 20/03/2020-19/04/2021 (HIRP, first lockdown to end of last lockdown), and 20/04/2021-03/06/2021 (LIRP). Among multiple gestations, we analyzed only the first newborn. Outcomes included PTB rate, delivery mode and neonatal outcomes. We further analyzed PTB rate in the following population subsets: terminations of pregnancy (TOP) excluded, singleton gestations and nulliparous. Periods comparisons were performed using one-way ANOVA test and Kruskal-Wallis test, as appropriate. A two-sided $p < 0.05$ defined statistical significance. The institutional review board approved this study and informed consent was waived (7068-20-SMC, 03/30/2020).

RESULTS

There were 10,707, 11,494, and 1330 deliveries in the pre-pandemic, HIRP and LIRP, respectively. Maternal and pregnancy characteristics were similar between groups (Table 1). Delivery rate at <37, <34, and <32 weeks of gestation was lower in the HIRP compared with the pre-pandemic and the LIRP ($p = 0.036$, $p = 0.015$, and $p = 0.004$, respectively, Table 1). Delivery mode and composite neonatal outcome were comparable between groups. Birthweight was lower in the pre-pandemic period compared with the HIRP ($p = 0.023$). In an analysis of the population subset of TOP excluded, there was a lower PTB rate (<37, <34 and <32) in the HIRP as compared to pre-pandemic and LIRP ($p = 0.041$, $p = 0.013$ and $p = 0.003$, respectively). The lower PTB rate in the HIRP as compared to the two other periods was demonstrated in an analysis of the subsets of nulliparous women (<34 and <32 weeks, $p = 0.009$ and $p = 0.007$, respectively) and singletons (<37, <34 and <32 weeks, $p = 0.010$, 0.014, $p = 0.012$, respectively) as well.

CONCLUSION

This study demonstrates a rebound increase in PTB rate during a Covid-19 LIRP, following a marked decrease in PTB rate during a HIRP. The lower PTB rate was observed across different gestational ages and among various subpopulations examined.

Our results strengthen previous publications that associated the Covid-19 pandemic to decreased PTB rates [3, 4]. As all our subanalyses resulted in the same trend, especially the nulliparous cohort which is considered to entail the lower risk of bias regarding obstetrical history, it is possible that the exposure to the period itself, as a complex interaction of multiple factors, is the basis for PTB rate change.

We found similar proportions of labor induction and preeclampsia across study groups. This finding suggests that iatrogenic deliveries have a low effect on overall PTB rate, further strengthening the hypothesis that the exposure to the high infection rate period itself has a substantial role in PTB.

The mode of delivery, both cesarean delivery and operative vaginal delivery rate, was similar across study periods. This finding strengthens the assumption that peripartum providers' care was not affected by exposure to a specific period in relation to the pandemic, despite increased physical and professional stress and professional burnout during the pandemic [5].

Limitations of this study include its retrospective design, limiting the possibility to establish a causality of the associations found. Furthermore, the single-center source of data might hamper the generalizability of our study results and limits the cohort's sample size. Finally, it is possible that unexamined factors (e.g., change in medical care providers, seasonal effects) could influence the outcomes. Of note, the study design aimed to minimize seasonal effects by comparing parallel periods.

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Table 1. Comparison of maternal clinical parameters, delivery and neonatal outcomes between the periods.

	Pre-pandemic period ($n = 10,707$)	High infection rate period ($n = 11,494$)	Low infection rate period ($n = 1330$)	*p* value
Age, mean (SD), years	32 ± 5.4	32 ± 5.3	32 ± 5.1	0.87
Body mass index, mean (SD), kg/m^2	28.4 ± 4.6	28.4 ± 4.6	28.4 ± 4.5	0.517
Weight gain, mean (SD), kg	12.6 ± 5.7	12.8 ± 5.7	12.9 ± 5.6	0.105
Nulliparous, No. (%)	3771 (35.2)	4074 (35.4)	483 (36.3)	0.723
Multiple gestation, No. (%)	421 (3.9)	464 (4.0)	56 (4.2)	0.851
Smoking, No. (%)	414 (3.9)	450 (3.9)	48 (3.6)	0.895
Covid-19 infection, No. (%)	–	260 (2.2)	49 (3.7)	0.002
Stillbirth, No. (%)	102 (1.0)	95 (0.8)	12 (0.9)	0.605
Termination of pregnancy, No. (%)	61 (0.6)	59 (0.5)	8 (0.6)	0.814
Preeclampsia, No. (%)	97 (0.9)	121 (1.1)	10 (0.8)	0.38
Hemoglobin level before delivery, mean (SD), g/dL	12.09 ± 1.1	12.20 ± 1.1	12.13 ± 1.1	<0.001
Induction of labor at <37$^{0/7}$[b]				
Vaginal prostaglandin, No. (%)	23 (2.2)	23 (2.3)	3 (2.5)	0.978
Intracervical balloon, No. (%)	75 (7.1)	70 (6.9)	7 (5.7)	0.847
Spontaneous rupture of membranes[a], No. (%)	401 (38.1)	375 (37.0)	39 (32.0)	0.401
Gestational age at delivery, mean (SD), weeks	38$^{6/7}$ ± 2$^{1/7}$	39$^{0/7}$ ± 1$^{6/7}$	38$^{6/7}$ ± 2$^{1/7}$	0.056
<37$^{0/7}$, No. (%)	1052 (9.8)	1014 (8.8)	122 (9.2%)	0.036
<34$^{0/7}$, No. (%)	285 (2.7)	238 (2.1)	32 (2.4)	0.015
<32$^{0/7}$, No. (%)	173 (1.6)	127 (1.1)	20 (1.5)	0.004
Gestational age at delivery excluding termination of pregnancy, mean (SD), weeks	39$^{0/7}$ ± 2$^{0/7}$	39$^{0/7}$ ± 1$^{5/7}$	39$^{0/7}$ ± 2$^{0/7}$	0.095
<37$^{0/7}$, No. (%)	993 (9.3)	957 (8.4)	114 (8.6)	0.041
<34$^{0/7}$, No. (%)	233 (2.2)	188 (1.6)	26 (2.0)	0.013
<32$^{0/7}$, No. (%)	127 (1.2)	85 (0.7)	14 (1.1)	0.003
Operative vaginal delivery, No. (%)	778 (7.3)	842 (7.3)	117 (8.8)	0.125
Cesarean delivery, No. (%)	3,038 (28.4)	3,199 (27.8)	395 (29.7)	0.301
Neonatal outcomes				
Birthweight, mean (SD), g	3161 ± 560	3182 ± 532	3174 ± 778	0.023
Composite neonatal outcome[b], No. (%)	599 (5.6)	601 (5.2)	59 (4.4)	0.15
Death within 24 hours from delivery, No. (%)	6 (0.1)	4 (0.01)	1 (0.1)	0.667
Mechanical ventilation, No. (%)	118 (1.1)	136 (1.2)	15 (1.1)	0.85
Hypoxic ischemic encephalopathy, No. (%)	10 (0.1)	13 (0.1)	3 (0.2)	0.389
Convulsions, No. (%)	19 (0.2)	18 (0.2)	0 (0.0)	0.305
Asphyxia, No. (%)	2 (0.01)	4 (0.01)	2 (0.2)	0.074
Apgar 1 min <5, No. (%)	44 (0.4)	62 (0.5)	4 (0.3)	0.246
Apgar 5 min <7, No. (%)	39 (0.4)	35 (0.3)	7 (0.5)	0.379
Arterial pH <7.0, No. (%)	29 (0.3)	39 (0.3)	1 (0.1)	0.204
Neonatal intensive care unit admission, No. (%)	508 (4.7)	505 (4.4)	42 (3.2)	0.025

[a]The rate is calculated out of all deliveries at <37$^{0/7}$.
[b]Composite neonatal outcome consisted of any of the following: stillbirth, neonatal death within 24 h from delivery, need for mechanical ventilation, hypoxic-ischemic encephalopathy, asphyxia, Apgar 1 min < 5 and 5 min < 7, arterial pH <7.0 and neonatal intensive care unit admission.

The main strength of this study is the evaluation of the period of emergence out of a high Covid-19 infection rate period, the examination of the population subsets including rates of stillbirths and TOP, and the analysis of multiple gestations and mode of delivery onset. Another advantage is the meticulous neonatal outcome analysis.

Our findings suggest that worldwide emergence from high infection periods during the pandemic could be associated with a return to pre-pandemic PTBs rates.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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AUTHOR CONTRIBUTIONS

GL and RM reviewed the literature and wrote the paper. RM and LF treated the patients and collected data. All authors read, revised, and approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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