BRIEF COMMUNICATION

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

Raanan Meyer1,2,3✉, Lior Friedrich4 and Gabriel Levin5,6

© The Author(s), under exclusive licence to Springer Nature America, Inc. 2022

Journal of Perinatology (2023) 43:670–672; https://doi.org/10.1038/s41372-022-01501-7

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 (PTBs) 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.

1The Department of Obstetrics and Gynecology, the Chaim Sheba Medical Center, Ramat-Gan, Israel. 2The Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel. 3The Sheba Talpiot Medical Leadership Program, the Chaim Sheba Medical Center, Ramat-Gan, Israel. 4The Joyce & Irving Goldman Medical School, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel. 5The Department of Obstetrics and Gynecology, Hadassah Medical Center, Jerusalem, Israel. 6The Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel. ✉email: raanameyer@gmail.com

Received: 30 June 2022 Revised: 15 August 2022 Accepted: 22 August 2022
Published online: 2 September 2022
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.

**REFERENCES**

1. Yang J, D’Souza R, Kharrat A, Fell DB, Snegrovel JW, Shah PS. COVID-19 pandemic and population-level pregnancy and neonatal outcomes in general population: a living systematic review and meta-analysis (Update#2: November 20, 2021). Acta Obstet Gynecol Scand. 2022;101:273–92.

---

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

| Parameter | 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/m² | 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 <37⁰/⁰

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, No. (%) | 401 (38.1) | 375 (37.0) | 39 (32.0) | 0.401 |
| Gestational age at delivery, mean (SD), weeks | 38⁰/⁰ ± 2⁰/⁷ | 39⁰/⁰ ± 1⁰/⁶⁷ | 38⁰/⁰ ± 2⁰/⁷ | 0.056 |
| <37⁰/⁰, No. (%) | 1052 (9.8) | 1014 (8.8) | 122 (9.2%) | 0.036 |
| <34⁰/⁰, No. (%) | 285 (2.7) | 238 (2.1) | 32 (2.4) | 0.015 |
| <32⁰/⁰, No. (%) | 173 (1.6) | 127 (1.1) | 20 (1.5) | 0.004 |
| Gestational age at delivery excluding termination of pregnancy, mean (SD), weeks | 39⁰/⁰ ± 2⁰/⁷ | 39⁰/⁰ ± 1⁰/⁷ | 39⁰/⁰ ± 2⁰/⁷ | 0.095 |
| Birthweight, mean (SD), g | 3161 ± 560 | 3182 ± 532 | 3174 ± 778 | 0.023 |
| Composite neonatal outcome, 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 |

*The rate is calculated out of all deliveries at <37⁰/⁰.*

*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.*
2. Israel Ministry of Health. COVID-19 virus in Israel 2021. https://datadashboard.health.gov.il/COVID-19/general.
3. Simon E, Cottenet J, Mariet AS, Bechraoui-Quantin S, Rozenberg P, Gouyon JB, et al. Impact of the COVID-19 pandemic on preterm birth and stillbirth: a nationwide, population-based retrospective cohort study. Am J Obstet Gynecol. 2021;225:347–8.
4. Lemon L, Edwards RP, Simhan HN. What is driving the decreased incidence of preterm birth during the coronavirus disease 2019 pandemic? Am J Obstet Gynecol MFM. 2021;3:100330.
5. Denning M, Goh ET, Tan B, Kanneganti A, Almonte M, Scott A, et al. Determinants of burnout and other aspects of psychological well-being in healthcare workers during the Covid-19 pandemic: a multinational cross-sectional study. PLoS ONE. 2021;16:e0238666.

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
Correspondence and requests for materials should be addressed to Raanan Meyer.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.