



Association between COVID-19 mandatory lockdown and decreased incidence of preterm births and neonatal mortality

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To the Editor

Previous studies suggest a decrease in preterm births (PTB) during de coronavirus disease 2019 (COVID-19), possibly due to the effect of the mandatory lockdown [1–6]. Nevertheless, other reports have been unable to confirm this finding [1, 7, 8]. Most of these studies originated in high-income countries and evaluated a limited number of potential confounders, and all of them assessed a short lockdown period. In addition, an important question remains unanswered: How can we be sure that the observed changes are due to lockdown, when most of the pregnancies delivered in the lockdown period were conceived prior to it?

To date there is insufficient evidence to support the notion that public health interventions during the lockdown prevent PTB [1]. The aim of this study was to compare the

incidence of PTB, neonatal mortality (NM) and stillbirths adjusted by potential confounders during the lockdown period assessing a time window of nine and a half months during which all the pregnancies analyzed in the exposed group were conceived after the lockdown, with the corresponding incidence in the previous year where all the unexposed pregnancies analyzed were conceived before the lockdown.

This is a multicenter retrospective analytic study. Data were extracted from medical records in 10 birth centers in Cordoba, Argentina. Two time periods were examined: August 13 to December 31, 2020 (exposed to lockdown), and August 13 to December 31, 2019 (unexposed to lockdown). This time window allows the study to include all pregnancies conceived from the beginning of the lockdown in the exposed period. The inclusion criteria were all singleton live birth infants from 22 weeks of gestation onwards. Multiple pregnancies and major congenital malformations were excluded.

Main outcomes included PTB, NM and stillbirths. PTB (<37, <34 and <32 weeks) were categorized as spontaneous or medically indicated preterm birth. The main exposure of interest was the mandatory lockdown. The covariates included in the analysis as possible confounders are listed in Table 1.

To compare outcomes between the groups we used Chi square test and student *t*-test. Crude and adjusted Odds Ratios with 95% Confidence Interval were calculated in a multivariate analysis using logistic regression.

Studies based on hospital registers do not require further Ethics Committee approval to comply with Argentine regulations.

16,555 singleton infants were born in the 10 centers analyzed, 8437 in the pre-lockdown unexposed period and 8118 in the lockdown exposed period.

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Table 1 Comparison of neonatal, delivery, maternal and fetal characteristics between the group exposed to mandatory lockdown (from August 13, 2020 to December 31, 2020) and the unexposed group during pre-lockdown period (from August 13, 2019 to December 31, 2019).

Variable	Exposed <i>n</i> (%) or mean (sd)	Unexposed <i>n</i> (%) or mean (sd)	Difference	95% CI	<i>p</i>
Single births	8118 (49.0)	8437 (51.0)			
Neonatal characteristics					
Birth weight	3240.6	3205.8	34.7	(19.30, 50.20)	<0.01
Grams (mean ± sd)	(506.6)	(506.5)			
Gestational age	39.4	39.1	0.3	(0.21, 0.33)	<0.01
Weeks (mean ± sd)	(2.0)	(1.9)			
Male sex	4165 (51.3)	4320 (51.2)	0.1	(−1.42, 1.63)	0.89
Preterm birth	690	806	−1.1	(−1.93, −0.18)	0.02
<37 weeks	(8.5)	(9.6)			
Preterm birth	282	376	−1.1	(−1.58, −0.39)	<0.01
<34 weeks	(3.5)	(4.6)			
Preterm birth	78	148	−0.8	(−1.15, −0.44)	<0.01
<32 weeks	(1.0)	(1.8)			
Neonatal deaths	37 (0.5)	84 (1.0)	−0.5	(−0.80, −0.28)	<0.01
Delivery characteristics					
Birth in Public Center	4774 (58.8)	4885 (57.9)	0.9	(−0.59, 2.41)	0.24
Cesarean delivery	3921 (48.3)	4202 (49.8)	−1.5	(−3.03, 0.02)	0.05
Medically indicated preterm birth (<37 weeks)	348 (4.3)	444 (5.3)	−1.0	(−1.62, −0.33)	<0.01
Spontaneous preterm birth (<37 weeks)	342 (4.2)	363 (4.3)	−0.1	(−0.70, 0.53)	0.78
Medically indicated preterm birth (<34 weeks)	130 (1.6)	188 (2.2)	−0.6	(−1.04, −0.21)	<0.01
Spontaneous preterm birth (<34 weeks)	152 (1.9)	188 (2.2)	−0.3	(−0.79, 0.08)	0.11
Maternal and fetal characteristics					
Maternal diabetes	438 (5.3)	472 (5.8)	−0.5	(−0.89, 0.50)	0.57
Maternal hypertension	414 (5.1)	422 (5.0)	0.1	(−0.57, 0.77)	0.77
Nulliparity	3190 (39.3)	3117 (40.5)	−1.2	(−2.70, 0.29)	0.11
Maternal age	28.6	28.6	0.0	(−0.20, 0.20)	0.99
Years (mean ± sd)	(6.3)	(6.3)			
Single mother	901 (11.5)	987 (11.7)	−0.6	(−1.57, 0.37)	0.22
Maternal education	1323	1358	0.2	(−0.92, 1.32)	0.73
<12 years	(16.3)	(16.1)			

Table 1 (continued)

Variable	Exposed n (%) or mean (sd)	Unexposed n (%) or mean (sd)	Difference	95% CI	p
Prenatal care <8 visits	414 (5.1)	413 (4.9)	0.2	(-0.46, 0.87)	0.55
Cigarette smoking	1275 (15.7)	1316 (15.6)	0.1	(-1.00, 1.22)	0.85
Fetal characteristics					
Stillbirths	57 (0.7)	67 (0.8)	0.1	(-0.30, 0.20)	0.49

Table 2 Association between the mandatory lockdown period and neonatal outcomes, unadjusted and adjusted by multiple logistic regression.

Variable	Crude Odds ratio (95% CI)	Adjusted Odds ratio (95% CI)	Adjusted difference (95% CI)	p
Neonatal characteristics				
Birth weight	-	1.00 (0.99, 1.00)	-	0.96
Gestational age	-	3.46 (2.92, 4.1)	-	<0.01
Preterm birth <37 weeks	0.88 (0.79,0.98)	0.89 (0.80, 0.99)	-1.0 (-1.82, -0.10)	<0.01
Preterm birth <34 weeks	0.77 (0.66,0.90)	0.83 (0.56,1.24)	-0.8 (-2.04, 1.10)	0.37
Preterm birth <32 weeks	0.54 (0.41,0.72)	0.58 (0.26, 1.30)	-0.8 (-1.33, 0.54)	0.18
Neonatal deaths	0.46 (0.31,0.67)	0.52 (0.41, 0.63)	-0.5 (-0.57, -0.38)	<0.01
Delivery characteristics				
Cesarean delivery	0.94 (0.89,1.00)	0.99 (0.90,1.09)	-0.5 (-4.98, 4.48)	0.83
Medically indicated preterm birth (<37 weeks)	0.81 (0.7,0.93)	0.79 (0.54, 1.14)	-1.1 (-2.44, 0.74)	0.22
Medically indicated preterm birth (<34 weeks)	0.71 (0.57,0.89)	0.39 (0.23, 0.65)	-1.3 (-1.69, -0.77)	<0.01

The comparison of sample characteristics between the exposed and the unexposed groups is depicted in Table 1. The lockdown period was related to a significant increment in birth weight and gestational age (GA) at birth. Neonatal male sex rate was similar in both periods. Preterm birth rates at <37, <34 and <32 weeks of gestation and NM rate were

significantly lower in the lockdown period than in the pre-lockdown period. Cesarean delivery rates and medically indicated PTB in the lockdown period reduced significantly compared with the pre-lockdown period. There were no differences in public birth rates, spontaneous PTB, maternal diabetes, maternal hypertension, nulliparity, maternal age, being a single mother, maternal education, prenatal visits, cigarette smoking and stillbirths between both periods.

Multivariate analysis shows that childbirth during the mandatory lockdown period was significantly associated with a decreased risk of PTB and NM. The observed risk reductions were dependently related to a reduction in medically indicated PTB and to increased GA during the mandatory lockdown period (Table 2).

Our findings were consistent with most previous studies that found decreases in PTB following the COVID-19 lockdown. Our finding lies principally in PTB <37 weeks of gestation and not only in PTB <34 or <32 weeks of gestation as in most of the other studies [1–6]. These differences are probably due to differences in the duration of the lockdown time under analysis as well as to differences in management and medical care resources between Argentina and the other countries. It is possible that during the lockdown, high risk pregnancies simply deferred labor for the protective effect of the lockdown and shifted from very PTB to moderate or late PTB. This hypothesis would explain why in our study the protective effect of the lockdown had much greater relative importance in PTB <37 weeks.

The observed reduction in PTB in our study was related to medically indicated PTB reduction and to GA increment during the lockdown period. We suggest that this finding may be related to the lower cesarean section rates occurring during the lockdown period. Two previous studies reported no change and one a significant decrease in PTB, greater in medically indicated than spontaneous PTB [1, 5, 7].

Our results differ from other studies that found no reduction or even reported an increase in PTB and NM [1, 7, 8].

The differences could be explained by differences in risk factors for adverse birth outcomes between countries, and by the differences in COVID-19 pandemic mitigation policies implemented by each country.

We found a significant decrease in the NM, possibly related to the considerable increase in chances of survival resulting from the increasing GA at delivery during the lockdown. This finding appears to be a solid result supporting the protective effect of the lockdown on maternal and neonatal health and wellbeing. Two previous studies have addressed NM. One that does not report changes between pre-lockdown and lockdown periods and another that reports an increase during COVID-19 pandemic [1, 6]. These differences are probably due to cultural, social and economic differences as well as to differences in management and medical care resources between countries. It is possible that some pregnancies have resulted in intrauterine death [1, 9, 10]. We did not find significant differences in the incidence of stillbirths during the lockdown period compared with the same period in the previous year, even adjusting by prenatal visits.

The major limitation of this study is the retrospective design. Future studies are needed to quantify the potential benefit that changes in working conditions, reduced exposure to infectious agents and environmental pollutants can have in reducing PTB.

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Author contributions EC conceptualized and designed the study, coordinated and supervised data collection, carried out the final data analyses, drafted the initial manuscript, and reviewed and revised the final manuscript. MEG-F, MDC, AJP, CM, IS-B, VB, GG, ME, SDB-P, DGP, LAA, RDP, AR, JIB, MBV, MJM, MF, GCM, HP and MR-R designed the data collection instruments, manually collected data, carried out the initial analyses, and reviewed and revised the manuscript for important intellectual content. All authors have approved the final manuscript as submitted.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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