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Danish premature birth rates during the COVID-19 lockdown

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ABSTRACT

To explore the impact of COVID-19 lockdown on premature birth rates in Denmark, a nationwide register-based prevalence proportion study was conducted on all 31 180 live singleton infants born in Denmark between 12 March and 14 April during 2015–2020.

The distribution of gestational ages (GAs) was significantly different (p=0.004) during the lockdown period compared with the previous 5 years and was driven by a significantly lower rate of extremely premature children during the lockdown compared with the corresponding mean rate for the same dates in the previous years (OR 0.09, 95% CI 0.01 to 0.40, p<0.001). No significant difference between the lockdown and previous years was found for other GA categories.

The reasons for this decrease are unclear. However, the lockdown has provided a unique opportunity to examine possible factors related to prematurity. Identification of possible causal mechanisms might stimulate changes in clinical practice.

What is already known on this topic?

- Prematurity, particularly extreme prematurity, has a high morbidity, and is considered the primary cause of mortality in children under 5 years old.
- Global overall prematurity rates are approximately 10%, but a large regional variation exists.
- The aetiology of preterm labour and premature birth is multifaceted and linked to a wide range of sociodemographic, medical, obstetric, foetal, psychosocial and environmental factors.

What this study adds?

- The rate of extremely premature birth decreased during the COVID-19 lockdown.
- Elements of the lockdown (eg, reduced infection load and reduced physical activity) are possibly beneficial for reducing extreme prematurity and potentially reducing infant mortality.

INTRODUCTION

COVID-19 was declared a pandemic on 12 March 2020, which led to an almost global lockdown. Beyond controlling transmission of the virus, the lockdown has affected virtually all branches of medicine and brought about changes in patterns of hospital contacts for other conditions. Although perinatal death has been reported, most severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive neonates appear to be only mildly affected,[1] and the majority of SARS-CoV-2-infected pregnancies do not develop major complications.[1]

Prematurity is a complex and challenging patho-physiological condition associated with increased risk of long-term morbidity and mortality, and it is the leading cause of death in children under 5 years of age.[2] Global prematurity rates are approximately 10% but vary from 4%-5% in some European countries to 15%-18% in some parts of Africa and Asia.[2] The aetiology of premature birth and preterm labour is multifaceted and linked to a wide range of sociodemographic, medical, obstetric, foetal, psychosocial and environmental factors.[3] Still, approximately two-thirds of premature births occur without an evident risk factor.[3]

In Denmark, a nationwide lockdown was declared on 12 March 2020. Effective from that date, childcare facilities, schools and universities were closed; all non-essential public servants were sent home; private employers were urged to ensure that as many people as possible worked from home; gatherings of over 10 people were prohibited; and the borders were closed to foreign visitors. A gradual lifting of lockdown restrictions began on 15 April 2020.

Anecdotal observations from neonatal intensive care units suggested fewer extremely premature births during the lockdown period. This study aimed to elucidate, if the lockdown itself—with its changes in work environment, social interactions and focus on hygiene (effectively reducing exposure to infectious agents)—impacted premature birth rates.

METHODS

We performed a nationwide prevalence proportion study with premature births as cases, term pregnancies as controls and birth during the lockdown period as exposure. Children born in Denmark during the most rigorous part of the lockdown period (12 March–14 April 2020) and in the previous 5 years (2015–2019) were identified from the Danish Neonatal Screening Biobank (DNSB).

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We also identified children from the period of 20 January–22 February, for years 2015–2020 (n=32 070), to analyse a period before COVID-19 had been reported in Denmark.

To limit the influence of other determinants of premature birth, we considered only singletons. Gestational age (GA) at birth was categorised in completed weeks (table 1).

Likelihood ratio-based tests, estimates and CIs regarding changes in composition of GA at birth categories between the lockdown period and the consolidated reference period for 2015–2019 were obtained from a series of logistic regressions. First, we made an assessment of the odds of being born during lockdown by GA category; that is, did the proportions in different GA categories vary by time? Second, on finding such variation, we estimated ORs of being in lockdown between each GA category and the rest, to possibly pinpoint GA categories with big relative changes. Frequency plots were used to illustrate variations in GA between the birth cohorts studied. Statistical analyses were run in SAS V.9.4 and R V.3.6.1.

RESULTS

We included 31 180 live singleton infants born in Denmark from 12 March to 14 April during 2015–2020. Births were distributed into GA categories (table 1). The total number of singleton births during lockdown in 2020 (n=5162) did not differ statistically significantly from the other years (mean births per year: 5203.6, SD ±221.4; p=0.24). We identified 1566 singleton premature infants (5.02%).

Logistic regression analyses demonstrated that the distribution of GA in 2020 differed significantly from the previous years (p=0.004). The proportion of extremely and very premature births (figure 1) was significantly different between the 2020 nationwide lockdown and the same calendar period from the previous 5 years (p=0.003). However, the difference was driven by a reduction in extremely premature to 0.19/1000 births during the 2020 nationwide lockdown compared with an average of 2.19/1000 births for the previous years (p<0.001) (table 1 and figure 1). No differences in birth rates were noted in the January and February periods (figure 1, inset).

DISCUSSION

We report a potential effect of a nationwide lockdown on extremely premature birth rates. Although it is too early to draw definitive conclusions, we believe that these findings and their potential implications merit immediate dissemination. The COVID-19 lockdown has drastically changed our lives by changing our working environment, reducing physical interactions and increasing our focus on hygiene. This unusual situation is likely to have influenced several risk factors for premature birth.

Increased systemic maternal inflammation is an element of several risk factors, which, along with other immunologically mediated processes, are believed to play a part in the preterm birth syndrome.[4] Possibly, the increased focus on hygiene, strict physical distancing and home confinement have influenced the overall inflammatory state of pregnant women.

The literature on a potential link between work and premature birth is contradictory.[5] Although we currently have no national details of their occurrences, the potential reduced physical demands associated with work, travel and even reductions in minor accidents or other traumas could all be possible contributors.

We found no significant differences in the rates of the very premature, moderate premature, term or post-term births, which

Table 1 GA categories and the distribution of singleton births throughout the study periods (12 March–14 April 2015–2020); the distribution of births permille, by GA category for the lockdown period (12 March–14 April 2020) compared with consolidated data from 12 March–14 April 2015–2019

	GA		2015	2016	2017	2018	2019	2020	Prevalence (permille)				
	Weeks+days	Mean (SD)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	2015–2019 (SD)	2020	OR	95% CI	P value
Extremely premature	≤27+6	25.7 (1.31)	13 (0.27)	9 (0.17)	9 (0.17)	13 (0.24)	13 (0.25)	1 (0.02)	2.19 (0.47)	0.19	0.09	0.01 to 0.40	<0.001
Very premature	28+0–31+6	29.7 (1.07)	27 (0.56)	32 (0.60)	31 (0.59)	28 (0.52)	27 (0.52)	32 (0.62)	5.57 (0.36)	6.20	1.11	0.75 to 1.61	0.589
Moderate/late premature	32+0–36+6	34.9 (1.26)	203 (4.19)	224 (4.20)	235 (4.44)	215 (3.98)	238 (4.62)	216 (4.18)	42.85 (2.45)	41.84	0.98	0.84 to 1.13	0.742
Term	37+0–41+6	39.6 (1.15)	4512 (93.20)	4936 (92.59)	4914 (92.82)	5023 (93.05)	4752 (92.20)	4810 (93.18)	927.70 (3.96)	931.81	1.06	0.95 to 1.20	0.293
Late term	≥42+0	42.0 (0.16)	86 (1.78)	130 (2.44)	105 (1.98)	119 (2.20)	124 (2.41)	103 (2.00)	21.68 (2.82)	19.95	0.92	0.74 to 1.13	0.430
Total	all births	39.4 (1.81)	4841 (100)	5331 (100)	5294 (100)	5398 (100)	5154 (100)	5162 (100)	1000	1000			

GA, gestational age.

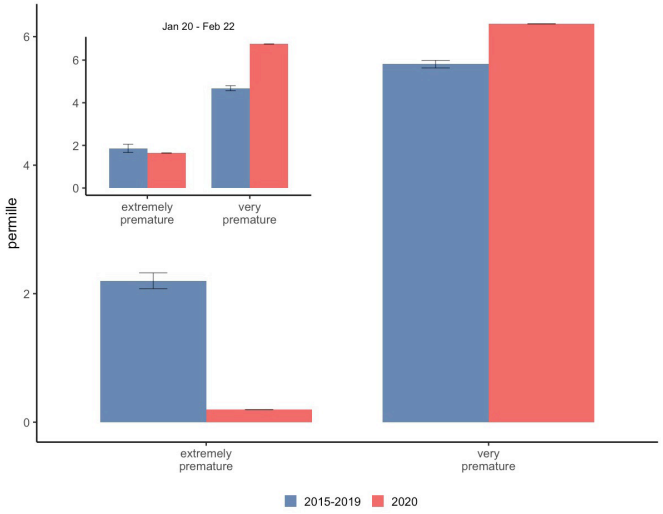

Figure 1 Proportion of extremely premature and very premature births (permille of all births in the time period) during the lockdown period (12 March–14 April 2020) compared with aggregated birth data for the previous 5 years during the same date range (12 March–14 April 2015–2019). Inset graph: a comparison of extremely premature and very premature births born between 20 January and 22 February 2020 and an aggregate from that date range for the previous 5 years (20 January–22 February 2015–2019). Extremely premature (before 28^{+0} weeks' gestation) and very premature (28^{+0}–31^{+6} weeks' gestation). Error bars represent 95% CIs.

may reflect that no such differences exist, or that the differences are too subtle to be detected. However, it is noteworthy that we observed a non-significant but slightly increased number of very premature births. It is possible that the impact lockdown had on risk factors for premature birth, served to simply postpone extremely preterm labour in some high-risk pregnancies, although this impact was not sufficient to avoid premature births altogether.

Our study has several strengths. Centralised neonatal screening has an uptake rate of nearly 100% in Denmark. Screening is performed within 3 days of birth, at the DNSB, which registers relevant clinical data pertaining to the birth, based on reliable, real-time, mandatory reporting. It is unlikely that the absence of extremely premature children is due to a decline in the rate of data transmission during the lockdown as no changes were detected in the other age categories. Because exposure (the lockdown) is independent of the recorded outcome, differential misclassification is not considered to be an issue. It is, however, possible that a larger than usual number of pregnancies resulted in intrauterine death, or that some extremely premature babies are missing due to early neonatal demise before registration with DNSB. Also, despite being a national study, the actual number of premature children remains small and must be interpreted with caution.

Importantly, this study is observational, and the association between the decreased number of extremely premature children and nationwide lockdown is not necessarily causal. As such, these data need to be confirmed in other countries, although international discrepancies regarding changes in premature birth rates could reflect the variation in baseline premature birth rates, as well as differences in implementation of lockdowns around the world. Future studies should also aim to elucidate potential causalities.

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Competing interests MB has a patent (NeoHelp) with royalties paid.

Patient consent for publication Not required.

Ethics approval Statens Serum Institut has approval from the Danish Data Protection Agency (DPA) to conduct register-based studies, and the current study was approved by the DPA officer (approval no: 20/04753) at Statens Serum Institut. Studies based solely on register data do not require further ethics committee approval as per Danish laws and regulations.

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