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ORIGINAL RESEARCH ARTICLE

SARS-CoV-2 infection in pregnancy in Denmark—characteristics and outcomes after confirmed infection in pregnancy: A nationwide, prospective, population-based cohort study

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Abbreviations: BMI, body mass index; CI, confidence interval; COVID-19, coronavirus disease 2019; DCOD, the Danish COVID-19 in pregnancy database; DNPR, The Danish National Patient Register; GA, gestational age in completed weeks; ICU, intensive care unit; LMP, date of the first day of the last menstrual period; MiBa, Danish Microbiology Database; NICU, neonatal intensive care unit; OR, crude odds ratio; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Abstract

Introduction: Assessing the risk factors for and consequences of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during pregnancy is essential to guide clinical care. Previous studies on SARS-CoV-2 infection in pregnancy have been among hospitalized patients, which may have exaggerated risk estimates of severe outcomes because all cases of SARS-CoV-2 infection in the pregnant population were not included. The objectives of this study were to identify risk factors for and outcomes after SARS-CoV-2 infection in pregnancy independent of severity of infection in a universally tested population, and to identify risk factors for and outcomes after severe infection requiring hospital admission.

Material and methods: This was a prospective population-based cohort study in Denmark using data from the Danish National Patient Register and Danish Microbiology Database and prospectively registered data from medical records. We included all pregnancies between March 1 and October 31, 2020 and compared women with a positive SARS-CoV-2 test during pregnancy to non-infected pregnant women. Cases of SARS-CoV-2 infection in pregnancy were both identified prospectively and through register linkage to ensure that all cases were identified and that cases were pregnant during infection. Main outcome measures were pregnancy, delivery, maternal, and neonatal outcomes. Severe infection was defined as hospital admission due to coronavirus disease 2019 (COVID-19) symptoms.

Results: Among 82 682 pregnancies, 418 women had SARS-CoV-2 infection during pregnancy, corresponding to an incidence of 5.1 per 1000 pregnancies, 23 (5.5%) of which required hospital admission due to COVID-19. Risk factors for infection were asthma (odds ratio [OR] 2.19, 95% CI 1.41–3.41) and being foreign born (OR 2.12, 95% CI 1.70–2.64). Risk factors for hospital admission due to COVID-19 included obesity (OR 2.74, 95% CI 1.00–7.51), smoking (OR 4.69, 95% CI 1.58–13.90), infection after gestational age (GA) 22 weeks (GA 22–27 weeks: OR 3.77, 95% CI 1.16–12.29; GA 28–36 weeks: OR 4.76, 95% CI 1.60–14.12), and having asthma (OR 4.53, 95% CI 1.39–14.79). We found no difference in any obstetrical or neonatal outcomes.

Conclusions: Only 1 in 20 women with SARS-CoV-2 infection during pregnancy required admission to hospital due to COVID-19. Risk factors for admission comprised obesity, smoking, asthma, and infection after GA 22 weeks. Severe adverse outcomes of SARS-CoV-2 infection in pregnancy were rare.

KEYWORDS
cohort studies, coronavirus disease 2019, obstetric delivery, pregnancy complications, pregnancy outcome, prospective studies, severe acute respiratory syndrome coronavirus 2

1 | INTRODUCTION

The World Health Organization declared a global pandemic of coronavirus disease 2019 (COVID-19) in March 2020.[1] COVID-19 is caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Assessing the risk factors for and consequences of infection with SARS-CoV-2 during pregnancy is essential to guide clinical guidelines and care.

Previous studies have identified risk factors for infection to include obesity, age, ethnicity, and pre-existing morbidities, and SARS-CoV-2 infection in pregnancy has been associated with an increased risk of admission to an intensive care unit (ICU), preterm delivery, and admission of the neonate to a neonatal intensive care unit (NICU).[2–6]

Most previous population-based studies on SARS-CoV-2 infection in pregnancy have been among hospitalized patients, which may exaggerate the risk estimates of severe outcomes because not all cases of SARS-CoV-2 infection in the pregnant population were included.[3,7] Only one study from the Netherlands included all cases independent of severity and hospital admission.[4] However, in that study, cases were identified prospectively in obstetric clinics, with the risk of selection bias. Additionally, the outcomes are in most studies compared with outcomes of historic cohorts of non-infected women, with the risk that the consequences of the pandemic will be attributed solely to SARS-CoV-2.[3,4,8] Lastly, testing strategies influence the estimated prevalence of SARS-CoV-2 infection, and potentially also the estimated severity of outcomes, if mild and asymptomatic cases are also detected.[2]

The testing strategy in Denmark rapidly evolved during the pandemic from testing the most ill in March 2020 to testing individuals with mild symptoms from April and testing close contacts from May. Universal testing of all pregnant women admitted to hospital including for delivery was implemented nationwide in early May 2020.

The objectives of this study were to identify risk factors for SARS-CoV-2 infection in pregnancy in a universally tested population and risk factors for severe infection requiring hospital admission, and to investigate the consequences of infection and severe infection on pregnancy, delivery, and neonatal outcomes when comparing with all non-infected pregnancies during the same time period.

2 | MATERIAL AND METHODS

This was a nationwide prospective population-based study investigating the association between SARS-CoV-2 infection in pregnancy and clinical characteristics and maternal, delivery, and neonatal outcomes. The study used prospectively registered data from medical records registered in the Danish COVID-19 in pregnancy database (DCOD) and register data obtained from the following national registers: the Danish National Patient Register (DNPR),[9] the Danish Microbiology Database (MiBa),[10] and the Civil Registration System.[11,12]

The overall study population was identified in DNPR and comprised all women registered with a pregnancy or birth-related International Classification of Diseases 10th revision diagnosis or procedure between March 1 and October 31, 2020 as specified in the Supporting Information Table S1. SARS-CoV-2-positive cases within the study population were identified by linkage to MiBa. In Denmark, all positive polymerase chain reaction (PCR) tests are registered in MiBa, but antigen and antibody tests were not during the study period. Pregnant women identified in the registers were followed up until December 11, 2020 considering all outcomes.

In the DCOD, women with a positive SARS-CoV-2 test during pregnancy between March 1 and October 31, 2020 were registered prospectively. Eligible SARS-CoV-2 tests included (a) PCR tests (of pharyngeal swab or tracheal secretion), (b) antigen tests (of nasal swab), or (c) detection of antibodies (IgG or total antibodies in serum) combined with a history of COVID-19 symptoms during pregnancy. The antibody assays used in Denmark have a high specificity and the risk of false positives is low;[13] a positive test was therefore considered inclusive. All obstetric units in Denmark reported to the DCOD based on data from prospectively collected medical records. DCOD was based in EasyTrial (easytrial.net, Denmark). To secure data completeness, cases were validated every second month by register linkage, with data obtained from the DNPR, Danish National Health Service Register,[14] and MiBa. The validation data set included only personal identification number, date of positive SARS-CoV-2 PCR test, date of hospital contact, and name of the hospital. Non-reported cases identified by validation who were pregnant at the time of a positive SARS-CoV-2 PCR test were entered into the DCOD retrospectively. Women included in the DCOD were followed up until data extraction on February 8, 2021.

The register data on the overall study population were pseudoanonymized, making it impossible to validate the SARS-CoV-2-positive cases from the registers against the DCOD cases on an individual level. We therefore present data for SARS-CoV-2-positive women from the DCOD alongside cases identified in the registers to illustrate the degree of comparability. SARS-CoV-2 cases in the DCOD and those registered in the national registers were each compared with the non-infected population. The validity of maternal and neonatal characteristics, surgical procedures, and main diagnoses in the Danish registers is considered high,[15] and we therefore evaluated that a comparison between the DCOD data and the register data was relevant.

The estimated date of delivery was registered in the DCOD and based on the first-trimester ultrasound examination offered to all pregnant women between gestational age (GA) 11 and 14 completed weeks. In case of first-trimester abortion, the estimated date of delivery was calculated based on the GA at abortion. In the DCOD, date of the first day of the last menstrual period (LMP) was defined as estimated date of delivery minus 280 days. In the register data, the LMP was calculated based on the registered GA at delivery or abortion. If still pregnant, we calculated the LMP based on GA at ultrasound examination, and if missing, the recommended GA for the registered ultrasound examinations. For abortions with a missing

registration of GA, GA was imputed based on the mean GA within the categories miscarriage or induced abortion.

Characteristics included maternal age at LMP, pre-pregnancy body mass index (BMI) based on the height and pre-pregnancy weight registered at first contact in pregnancy, smoking defined as any smoking during pregnancy, parity, multiple pregnancy, pre-eclampsia, gestational diabetes, and diabetes. The register data set also included pre-existing asthma and hypertension diagnosed within 5 years of LMP. Supporting information Table S2 presents the codes used to identify characteristics and outcomes in DNPR. The DCOD also included information on migrant status defined as not born in Denmark, employment status including ongoing education, asthma defined as asthma requiring steroid inhalation as registered in the Danish Shared Medication Record,[16] pre-existing medical problems and previous pregnancy-related complications as specified in Supporting information Table S3. GA at infection was calculated based on the date of the first positive SARS-CoV-2 test in the case of a PCR test or date of symptoms in the case of an antibody test.

Maternal outcomes included admission to an ICU, pneumonia (in the DCOD defined as confirmed by radiologic examination), thromboembolic events, maternal mortality (death during pregnancy or within 7 days postpartum) and pregnancy outcomes including delivery, termination of pregnancy before GA 23 weeks, or miscarriage before GA 22 weeks.

Delivery outcomes comprised mode of delivery, induction of labor, and preterm birth before GA 37 weeks.

Neonatal outcomes included admission to a NICU directly from the delivery or maternity ward, stillbirth from GA 22 weeks, Apgar score at 5 minutes, umbilical artery pH, and neonatal death (within 28 days postpartum).

Information on maternal and neonatal death was retrieved from the Danish Civil Registration System, which is considered highly valid and complete.[12]

Data on migrant status and infant admission to a NICU were not available in our register data. These variables registered in the DCOD were therefore compared with historical data comprising migrant status of all women with a liveborn child in 2019 as reported by Statistics Denmark[17] and admissions to an NICU of all live-born children in 2019 as reported by the Danish Quality Database for newborns.[18]

In the DCOD, admission to hospital with a concurrent SARS-CoV-2 infection was defined as admission and discharge on two different dates and a positive SARS-CoV-2 test within 14 days before or during admission. Severe infection was defined if admission to hospital was due to COVID-19 symptoms.

2.1 | Statistical analyses

Categorical variables are presented as count with percentage, and continuous variables as median with interquartile range. For DCOD data numbers less than 3 and for register data numbers less than 5 are not reported to avoid identification according to the respective ethical approvals. The categorical DCOD data were analyzed with chi-squared test when compared with the non-infected population, and with logistic regression when comparing severe and non-severe DCOD cases including multivariate analyses adjusting for the predefined risk factors age, BMI, parity, and smoking. Continuous DCOD variables were analyzed using the Wilcoxon signed rank test. We performed a sub-analysis of the DCOD cases testing for the influence of GA at time of SARS-CoV-2 infection on key outcomes comprising cesarean delivery, induction of labor, preterm birth, and NICU admission. In the analysis of register data, categorical outcomes were assessed with univariate and multiple logistic regression and continuous variables with linear regression. The multivariate analyses adjusted for (a) maternal age and LMP to adjust for time of inclusion in the study, and (b) predefined risk factors including maternal age, LMP, parity, BMI, and smoking. In the linear regression model, we included log-transformed outcome variables, applying bootstrapping to account for non-normal distribution of residuals. For the outcomes miscarriage, termination of pregnancy, and preterm delivery, a Cox regression analysis was performed, including SARS-CoV-2 as time-dependent exposure, to account for duration of exposure to SARS-CoV-2 during follow up. These analyses were performed with delayed entry to reduce the risk of immortal-time bias, which can occur when participants cannot experience the outcome during part of the follow-up time. For the first two outcomes, women were therefore included in the survival analysis according to the time of first registered hospital contact, and for preterm delivery, women were included at GA 100 days. SARS-CoV-2 exposure was registered at the date of positive test. Missing data were excluded from all analyses. A p-value of 0.05 or less was considered statistically significant. Data were analyzed using STATA/MP16 (64-bit; StataCorp) and SPSS statistics 27 (IBM).

2.2 | Ethical approval

The study was approved by the Danish Patient Safety Authority on April 24, 2020 (reg. no. 31-1521-252), the regional Data Protection Agency in Region Zealand on March 23, 2020 (reg. no. REG-022-2020), and the regional Data Protection Agency in the Region of Southern Denmark on April 15, 2020 (reg. no. 20/17416). Individual patient consent was not required. The study is reported according to STROBE guidelines.[19]

3 | RESULTS

Among 82 682 pregnancies in Denmark between March 1 and October 31, 2020, 420 women had a SARS-CoV-2 positive PCR test, and 418 SARS-CoV-2 cases were confirmed as being during pregnancy through validation against medical records. Figure 1A illustrates the flow through the register-based study, and Figure 1B the flow through the DCOD study.

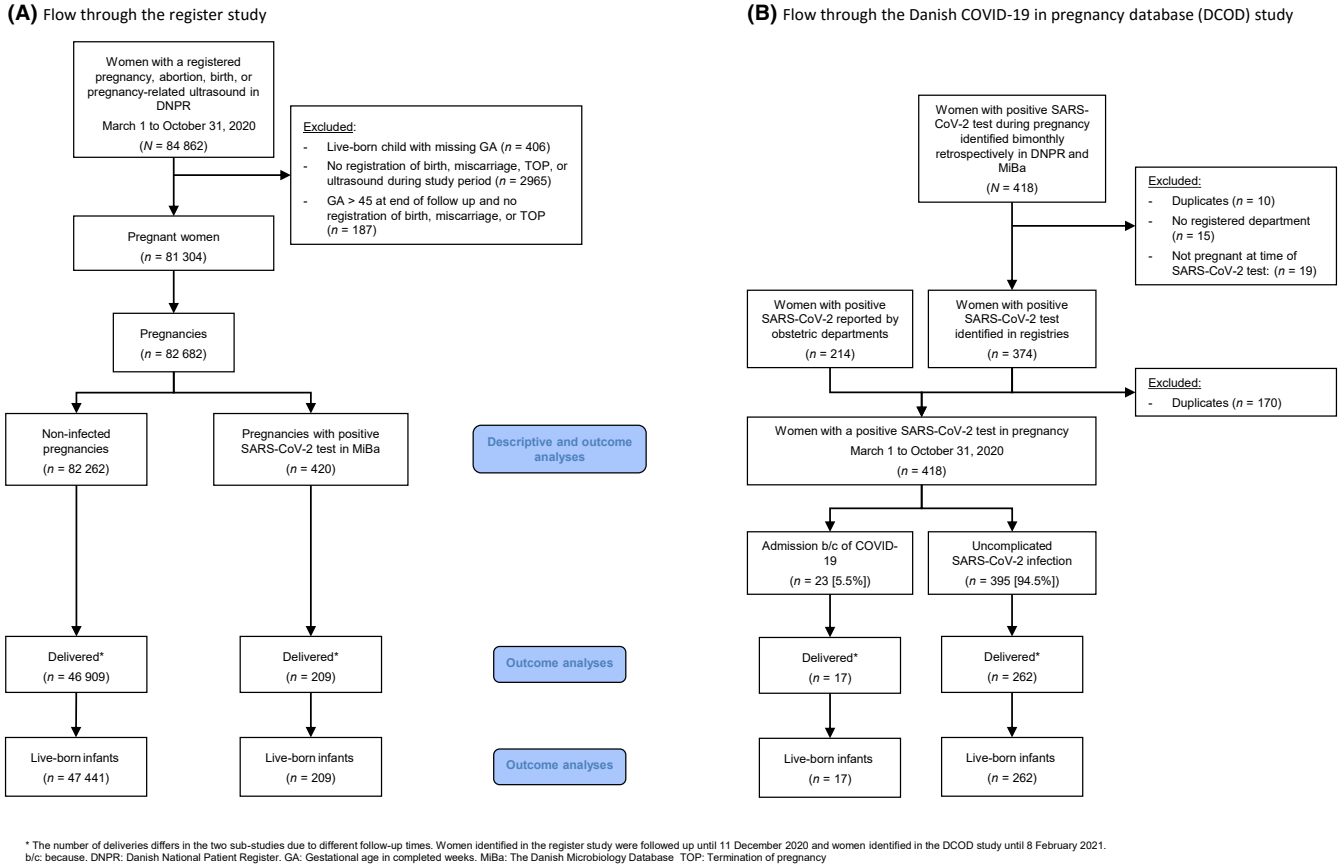

FIGURE 1 (A) Flowchart for the register study. (B) Flowchart for the Danish COVID-19 in pregnancy database (DCOD) study

The overall incidence of SARS-CoV-2 infection during validated pregnancy in the inclusion period was 5.1 (95% CI 4.7–5.5) per 1000 pregnancies, with the monthly incidence ranging from 0.2 per 1000 pregnancies in July to 3.8 per 1000 pregnancies in October (Supporting Information Figure S1). Of the SARS-CoV-2 cases in pregnancy, 23 (5.5%) were admitted to hospital because of COVID-19 symptoms.

Basic characteristics of women and their pregnancies according to SARS-CoV-2 status and severity of infection are presented in Table 1 and the Supporting Information Table S4. Pregnant women infected with SARS-CoV-2 more frequently had pre-existing asthma (crude odds ratio [OR] 2.19, 95% CI 1.41–3.41) and were foreign born (OR 2.12, 95% CI 1.70–2.64) compared with the non-infected. There were no differences in the rates of pre-eclampsia or gestational diabetes. Women who required admission to hospital had a significantly higher pre-pregnancy BMI (p = 0.018), were more likely to smoke (OR 4.69, 95% CI 1.58–13.90), and had pre-existing asthma (OR 4.53, 95% CI 1.39–14.79). Compared with women becoming infected before, women becoming infected after GA 22 weeks had a higher risk of COVID-19-related hospital admission (GA 22–27 weeks: OR 3.77, 95% CI 1.16–12.29; GA 28–36 weeks: OR 4.76, 95% CI 1.60–14.12).

The outcomes of the SARS-CoV-2-infected women compared with all non-infected pregnancies are presented in Table 2. The risk of pneumonia was significantly higher among SARS-CoV-2-infected pregnant women (OR 15.97, 95% CI 6.92–36.86). All cases of pneumonia (n = 6) were among women admitted to hospital because of COVID-19 and none of them smoked in pregnancy. The rate of thromboembolic events and admission to an ICU was low, and we had no cases of maternal death during the study period. The rate of early pregnancy loss did not vary between the groups after adjusting for exposure time. However, the risk of termination of pregnancy was increased after adjustment (hazard ratio 2.39, 95% CI 1.29–4.45) among the SARS-CoV-2-infected women. The median time between SARS-CoV-2 infection and delivery was 88 days (interquartile range 35–138). We found no difference between the groups regarding any of the delivery or infant outcomes. Adjustment did not change the results. There were no neonatal deaths among the children of SARS-CoV-2-infected women.

We found no statistically significant differences in outcomes between women requiring hospital admission due to COVID-19 symptoms compared with less severe SARS-CoV-2 cases (Table 3).

There was no difference in risk of cesarean delivery, induction of labor, preterm birth, or NICU admission in relation to GA at infection among the SARS-CoV-2-infected women (data not shown).

TABLE 1 Basic characteristics of SARS-CoV-2-infected women overall and according to severity of infection and all pregnant women in Denmark between March 1 and October 31, 2020

		SARS-CoV-2-infected pregnant women identified in DCOD	SARS-CoV-2-infected pregnant women/ pregnancies identified in the national registers[a]	Non-infected pregnancies identified in the national registers[a]	SARS-CoV-2-infected vs. non-infected pregnancies		SARS-CoV-2-infected women identified in DCOD			
					DCOD SARS-CoV-2 cases	Register SARS-CoV-2 cases	Women requiring admission to hospital due to COVID-19 symptoms	Women with uncomplicated SARS-CoV-2 infection[b]	Women requiring hospital admission due to COVID-19 symptoms vs. women with uncomplicated SARS-CoV-2 infection[b]	
		N = 418	*N* = 420	*N* = 82 262	OR_D (95% CI)	OR_R (95% CI)	*N* = 23	*N* = 395	OR_{DCOD} (95% CI)	*p*
Basic characteristics										
Age (years)	<25	51 (12.2)	48 (11.4)	10 324 (12.6)	1 (ref.)	1 (ref.)				
	25–34	291 (69.6)	297 (70.7)	57 372 (69.7)	1.02 (0.75–1.41)	1.11 (0.82–1.51)				
	≥35	76 (18.2)	75 (17.9)	14 566 (17.7)	1.05 (0.73–1.53)	1.11 (0.77–1.59)				
	≥30						10 (43.5)	185 (47.0)	0.87 (0.37–2.03)	
	Median	29.6 (27.0–33.4)	29.0 (27.0–33.0)	30.0 (27.0–33.0)	NA	0.99 (0.97–1.01)	29.9 (25.4–33.2)	29.5 (27.0–33.5)		0.750
BMI (kg/m^2)	<25 (normal)	241 (60.3)	113 (55.1)	27 083 (58.5)	1 (ref.)	1 (ref.)	10 (43.5)	231 (61.5)	1 (ref)	
	25 –29.9 (overweight)	93 (23.3)	61 (29.8)	11 904 (25.7)	0.88 (0.68–1.12)	1.23 (0.90–1.68)	6 (26.1)	87 (23.0)	1.60 (0.56–4.52)	
	≥30 (obese)						7 (30.4)	59 (15.6)	**2.74 (1.00–7.51)**	
	30–34.9 (obese)	44 (11.0)	23 (11.2)	4609 (9.9)	1.07 (0.75–1.48)	1.20 (0.76–1.87)				
	≥35 (obese)	22 (5.5)	8 (3.9)	2729 (5.9)	0.91 (0.56–1.41)	0.70 (0.34–1.44)				
	Unknown	18 (4.3)	215 (51.2)	35 937 (43.7)			0 (0)	18 (4.6)		
	Median	24.1 (26.9–33.4)	24.0 (22.0–27.0)	24.0 (21.0–27.0)	NA	1.01 (0.99–1.04)	25.6 (23.7–31.2)	24.0 (21.6–27.6)		**0.018**
Smoking	Smoking in pregnancy	27 (6.8)	10 (4.9)	3598 (7.9)	0.86 (0.58–1.27)	0.60 (0.32–1.13)	5 (22.7)	22 (5.9)	**4.69 (1.58–13.90)**	
	Unknown	23 (5.5)	214 (51.0)	36 478 (44.3)			1 (4.3)	22 (5.6)		
Pre-existing asthma		21 (5.2)	23 (5.5)	1996 (2.4)	**2.19 (1.41–3.41)**	**2.33 (1.53–3.56)**	4 (17.4)	17 (4.4)	**4.53 (1.39–14.79)**	
	Unknown	12 (2.9)					0 (0)	12 (3.0)		

(Continues)

TABLE 1 (Continued)

		SARS-CoV-2-infected pregnant women identified in DCOD	SARS-CoV-2-infected pregnant women/ pregnancies identified in the national registers[a]	Non-infected pregnancies identified in the national registers[a]	SARS-CoV-2-infected vs. non-infected pregnancies		SARS-CoV-2-infected women identified in DCOD			
					DCOD SARS-CoV-2 cases	Register SARS-CoV-2 cases	Women requiring admission to hospital due to COVID-19 symptoms	Women with uncomplicated SARS-CoV-2 infection[b]	Women requiring hospital admission due to COVID-19 symptoms vs. women with uncomplicated SARS-CoV-2 infection[b]	
		N = 418	*N* = 420	*N* = 82 262	OR_D (95% CI)	OR_R (95% CI)	*N* = 23	*N* = 395	OR_{DCOD} (95% CI)	*p*
Pre-existing medical problem[c]		82 (20.2)	NA	NA			8 (34.8)	74 (19.3)	2.23 (0.91–5.45)	
	Unknown	12 (2.9)					0 (0)	12 (3.0)		
Migrant[d]		119 (32.2)	NA	11 211 (18.3)	**2.12 (1.70–2.64)**	NA	10 (47.6)	109 (31.3)	1.99 (0.82–4.83)	
	Unknown	49 (11.7)					2 (8.7)	47 (11.9)		
COVID-19 characteristics										
GA at infection[e] (in completed weeks)	<22	191 (45.8)	211 (50.2)	NR			5 (21.7)	186 (47.2)	1 (ref)	
	22–27	76 (18.2)	77 (18.3)	NR			7 (30.4)	69 (17.5)	**3.77 (1.16–12.29)**	
	28–36	97 (23.3)	89 (21.2)	NR			11 (47.8)	86 (21.8)	**4.76 (1.60–14.12)**	
	37–	53 (12.7)	43 (10.2)	NR			0 (0.0)	53 (13.5)	NR	
	Unknown	1 (0.2)						1 (0.3)		
	Median	22^{+6} week (15^{+0}–30^{+4} week)	21^{+0} week (14^{+0}–29^{+0} week)	NR			26^{+4} week (23^{+4}–32^{+0} week)	22^{+1} week (14^{+4}–30^{+0} week)		0.093
Test type	PCR or antigentest	399 (97.3)	420 (100)	NR			23 (100)	376 (97.2)	1.03 (1.01–1.05)	
	Antibodies (IgG or total) in serum	11 (2.7)		NR			0 (0)	11 (2.8)	NR	
	Unknown	8 (1.9)					0 (0)	8 (2.0)	NR	
Pregnancy characteristics										

(Continues)

TABLE 1 (Continued)

		SARS-CoV-2-infected pregnant women identified in DCOD	SARS-CoV-2-infected pregnant women/ pregnancies identified in the national registers[a]	Non-infected pregnancies identified in the national registers[a]	SARS-CoV-2-infected vs. non-infected pregnancies		SARS-CoV-2-infected women identified in DCOD			
					DCOD SARS-CoV-2 cases	Register SARS-CoV-2 cases	Women requiring admission to hospital due to COVID-19 symptoms	Women with uncomplicated SARS-CoV-2 infection[b]	Women requiring hospital admission due to COVID-19 symptoms vs. women with uncomplicated SARS-CoV-2 infection[b]	
		N = 418	*N* = 420	*N* = 82 262	OR_D (95% CI)	OR_R (95% CI)	*N* = 23	*N* = 395	OR_{DCOD} (95% CI)	*p*
Parity	Multiparous	230 (56.7)	218 (53.7)	39 727 (55.1)	1.07 (0.88–1.30)	0.95 (0.78–1.15)	16 (69.6)	219 (56.4)	1.76 (0.71–4.39)	
	Unknown	12 (2.9)	14 (3.3)	10 156 (12.3)			0 (0)	7 (1.8)		
Multiple pregnancy		<3	<5	1005 (1.2)	NA	NA	0 (0)	<3		
	Unknown	4 (1.0)					0 (0)	4 (1.0)		
Pre-eclampsia/ Eclampsia		<3	6 (1.4)	1642 (2.0)	NA	0.71 (0.32–1.60)	NA	NA		
GDM		19 (4.5)	22 (5.2)	3353 (4.1)	1.12 (0.71–1.78)	1.30 (0.85–2.00)	<3	>16	NA	
Thromboembolic event		<3	0 (0.0)	62 (0.1)	NA	NR	0 (0)	<3	NA	

Note: Data are presented as count (%) or median (interquartile range). Significant results are highlighted in bold type.

OR_D was estimated using 2 × 2 contingency tables. OR_R was for categorical outcomes estimated using univariate logistic regression with the lowest value as the reference. OR_R was for continuous variables estimated using linear regression with the dependent variable log-transformed and the unexposed category as reference. OR_{DCOD} was estimated using logistic regression.

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; DCOD, Danish COVID-19 in pregnancy database; GA, gestational age; GDM, gestational diabetes mellitus; NA, not available; NR, not relevant; OR, odds ratio; PCR, polymerase chain reaction; SARS-CoV-2, severe acute repiratory syndrome coronavirus 2.

[a]The Danish national registers comprised the Danish National Patient Register (DNPR) and the Danish Microbiology Database (MiBa).

[b]Uncomplicated COVID-19 included cases where women did not require admission to hospital due to COVID-19 symptoms, and therefore included women in home isolation or women admitted for obstetrical reason within 14 days of first positive SARS-CoV-2 test or symptoms.

[c]Pre-existing medical problems included endocrine, cardiac, renal, psychiatric, hematological, inflammatory and autoimmune disease, and cancer and HIV.

[d]Migrant was defined as not born in Denmark. The comparator group was all women with a live-born child in 2019 in Denmark (*N* = 61,167) (Statistics Denmark, https://statistikbanken.dk/FODIE [accessed February 4, 2021]). Country of origin is specified in Supporting Information, Table S4.

[e]GA at infection was defined as date of first positive test in case of a PCR test or date of symptoms in case of an antibody test.

TABLE 2 Outcomes for women with SARS-CoV-2 infection in pregnancy compared to all pregnancies in Denmark between March 1 and October 31, 2020

			SARS-CoV-2-infected pregnant women identified in DCOD	SARS-CoV-2-infected pregnant women/ pregnancies identified in the national registers	Non-infected pregnancies identified in the national registers	SARS-CoV-2-infected vs. non-infected pregnancy[a]		
						DCOD SARS-CoV-2 cases	Register SARS-CoV-2 cases	
						OR_D (95% CI)	OR_R (95% CI)	HR_a (95% CI)
Maternal outcome			*N* = 418	*N* = 420	*N* = 82 262			
Pneumonia confirmed by radiologic examination			6 (1.5)	<5	77 (0.1)	**15.97 (6.92–36.86)**	NA	
	Unknown		11 (2.6)					
Admission[b] to hospital due to COVID-19			23 (5.5)	NA	NA	NA		
Admission[b] to hospital for any reason			65 (15.5)	NA	NA	NA		
Admission to intensive care unit			<3	<5	264 (0.3)	NA	NA	
	Unknown		33 (7.9)					
Death			0 (0)	0 (0.0)	0 (0.0)	NA	NA	
	Unknown		62 (14.8)					
Early pregnancy loss GA <22 weeks			11 (2.7)	11 (2.6)	6478 (7.9)	NR	NR	1.48 (0.82–2.67)
	Unknown		7 (1.7)					
	GA <12 weeks		6 (1.5)	>5	4736 (5.8)	NR	NA	
	GA 12–21 weeks		4 (1.0)	<5	1742 (2.1)	NR	NA	
	Missing information about GA		1 (0.2)					
Ectopic pregnancy			3 (0.7)	<5	512 (0.6)	1.15 (0.37–3.61)	NA	
Termination of pregnancy			11 (2.7)	10 (2.4)	5261 (6.4)	NR	NR	**2.49 (1.34–4.64)**
	Unknown		6 (1.4)					
	GA <12 weeks		6 (1.5)	>5	4929 (6.0)	NR	NA	
	GA 12–22 weeks		5 (1.2)	<5	332 (0.4)	NR	NA	
Delivery outcome								
Delivered[c]			*N* = 279	*N* = 209	*N* = 46 909			
Mode of delivery	Vaginal		221 (79.2)	169 (80.9)	37 467 (79.9)	0.96 (0.72–1.28)	1.06 (0.75–1.50)	
		Operative vaginal delivery	18 (6.5)	13 (6.2)	2583 (5.5)	1.18 (0.69–1.91)	1.14 (0.65–2.00)	
	Cesarean delivery (CD)		58 (20.8)	40 (19.1)	9442 (20.1)	1.04 (0.78–1.39)		
		Emergency CD	35 (12.5)	26 (12.4)	5368 (11.4)	1.11 (0.78–1.58)	1.10 (0.73–1.66)	
		Elective CD	23 (8.2)	14 (6.7)	3735 (8.0)	1.04 (0.68–1.59)	0.83 (0.48–1.43)	
Induction			72 (25.8)	47 (22.5)	10 314 (22.0)	1.23 (0.94–1.62)	1.03 (0.74–1.43)	

(Continues)

TABLE 2 (Continued)

		SARS-CoV-2-infected pregnant women identified in DCOD	SARS-CoV-2-infected pregnant women/ pregnancies identified in the national registers	Non-infected pregnancies identified in the national registers	SARS-CoV-2-infected vs. non-infected pregnancy[a]		
					DCOD SARS-CoV-2 cases	Register SARS-CoV-2 cases	
					OR_D (95% CI)	OR_R (95% CI)	HR_a (95% CI)
Preterm birth GA <37 weeks		13 (4.7)	12 (5.7)	2539 (5.4)	0.85 (0.49–1.49)	1.06 (0.59–1.91)	0.94 (0.47–1.88)
	Median (IQR)	40^{+0} weeks (39^{+1}–41^{+0} weeks)	39^{+6} weeks (38^{+6}–40^{+6} weeks)	40^{+1} weeks (39^{+0}–41^{+0} weeks)	NA	0.99 (0.98–1.00)	
Interval between COVID-19 and delivery (days), median (IQR)		88 (35–138)	76 (23–145)	NR			
Infant outcome							
IUFD		<3	<5	134 (0.3)	NA	NA	
Liveborn infants		*N* = 279	*N* = 209	*N* = 47 441			
NICU admission[d]		28 (10.0)		5514 (9.3)	1.09 (0.74–1.61)		
COVID-19 infection in neonate		0 (0.0)	NA	NA	NA		
	Unknown	26 (9.3)					
Congenital malformations		5 (1.8)	NA	NA	NA		
	Unknown	1 (0.4)					
Apgar at 5 min	<7	0 (0)	<5	482 (1.0)	NR	NA	
	Unknown	3 (1.1)	<5	768 (1.6)			
	Median	10 (10.0–10.0)	10.0 (10.0–10.0)	10.0 (10.0–10.0)	NA	1.00 (1.00–1.00)	
Umbilical cord pH (arterial)	<7.10	8 (3.6)	6 (3.8)	1408 (4.6)	0.77 (0.38–1.56)	0.81 (0.36–1.84)	
	Unknown	54 (19.4)	49 (23.4)	16 592 (35.0)			
	Median	7.24 (7.18–7.27)	7.2 (7.2–7.3)	7.2 (7.2–7.3)	NA	1.00 (1.00–1.00)	
Neonatal death		0 (0.0)	0 (0.0)	11 (0.0)	NA	NA	

Note: Data are presented as count (%) or median (interquartile range). Significant findings are highlighted in bold type.

Abbreviations: CD, cesarean delivery; COVID-19, coronavirus disease 2019; DCOD, Danish COVID-19 in pregnancy Database; GA, gestational age; GP, general practitioner; IQR, interquartile range; IUFD, intrauterine fetal death; NICU, neonatal intensive care unit; NR, not relevant; OR, odds ratio; SARS,CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]OR_D was estimated using 2 × 2 contingency tables. OR_R was for categorical outcomes estimated using univariate logistic regression with the lowest value as the reference. OR_R was for continuous variables estimated using linear regression with the dependent variable log-transformed and the unexposed category as reference. HRa was estimated by a Cox regression adjusting for exposure time for relevant variables and the unexposed category as reference. HRa was adjusted for age and first day of the last menstrual period.

[b]Admission to hospital with a concurrent SARS-CoV-2 infection was defined as admission and discharge on two different dates and a positive SARS-CoV-2 test within 14 days of admission.

[c]The proportion of women who had delivered at the time of analyses varied due to different follow-up time in DCOD and the register data (please see Material and methods section).

[d]The comparator group were live-born children who were admitted to a neonatal intensive care unit directly from a delivery or maternity ward and later discharged home or who died among all live-born children in Denmark in 2019 (*N* = 59 391). (Dansk Kvalitetsdatabase for Nyfødte [DKN]). Datakvalitetsrapport 2019. Pg. 30. Available at: Microsoft Word – 2021-02-03 DKN_Datarapport_officiel (sundhed.dk [accessed February 19, 2021]).

TABLE 3 Outcomes for women with severe COVID-19 infection requiring admission to hospital compared to less severe SARS-CoV-2 cases in pregnancy in Denmark between March 1 and October 31, 2020 as registered in the Danish COVID-19 in pregnancy database (DCOD)

		SARS-CoV-2-infected women registered in DCOD				
		Women requiring admission to hospital due to COVID-19 symptoms	Uncomplicated SARS-CoV-2 infection[a]			
		N = 23	*N* = 395	OR (95% CI)	*p*	aOR (95% CI)[b]
Maternal outcome						
		N = 23	*N* = 395			
Death		0 (0)	0 (0)	NR		
	Unknown	1 (4.3)	61 (15.4)			
Ectopic pregnancy		0 (0)	3 (0.8)	NR		
Termination of pregnancy GA <23 weeks		0 (0)	11 (2.8)	NR		
	Unknown	0 (0)	6 (1.5)			
Delivered		17 (73.9)	262 (66.3)	1.44 (0.55–3.73)		1.74 (0.62–4.93)
Delivery outcome						
Delivered		*N* = 17	*N* = 262			
Mode of delivery						
	Unassisted vaginal delivery	11 (64.7)	192 (73.3)	1 (ref)		1 (ref)
	Operative vaginal delivery	0 (0.0)	18 (6.9)	NR		NR
	Emergency CD	3 (17.6)	32 (12.2)	1.64 (0.43–6 19)		1.88 (0.46–7.74)
	Elective CD	3 (17.6)	20 (7.6)	2.62 (0.67–10.17)		3.81 (0.85–17.09)
Induction		7 (41.2)	65 (24.8)	2.12 (0.78–5.80)		1.53 (0.52–4.49)
Interval between COVID-19 and delivery (days)		62 (42–103)	91 (35–138)		0.250	
Infant outcome						
Liveborn infants		*N* = 17	*N* = 262			
GA at delivery		39^{+5} weeks (38^{+4}–40^{+5} weeks)	40^{+0} weeks (39^{+1}–41^{+0} weeks)		0.161	
Preterm birth GA <37 weeks		<3	>10	NA		
NICU admission		4 (23.5)	24 (9.2)	3.05 (0.92–10.10)		3.37 (0.95–11.97)
Gender	Boy	8 (47.1)	121 (46.2)	1.04 (0.39–2.77)		1.12 (0.40–3.15)
Weight at delivery (g)		3460 (3109–3810)	3475 (3198–3859)		0.733	
Apgar at 5 min	<7	0 (0)	0 (0)	NR		
	Unknown	0 (0.0)	3 (1.1)			
	Median	10 (10–10)	10 (10–10)		0.170	
Umbilical cord pH (arterial)	<7.10	0 (0.0)	8 (3.7)	NR		

(Continues)

TABLE 3 (Continued)

		SARS-CoV-2-infected women registered in DCOD				
		Women requiring admission to hospital due to COVID-19 symptoms	Uncomplicated SARS-CoV-2 infection[a]			
		N = 23	*N* = 395	OR (95% CI)	*p*	aOR (95% CI)[b]
	Unknown	6 (35.3)	48 (18.3)			
	Median	7.23 (7.17–1.28)	7.24 (7.18–7.27)		0.823	
Congenital malformations		0 (0.0)	5 (1.9)	NR		NR
	Unknown	0 (0.0)	1 (0.4)			
Neonatal death		0 (0.0)	0 (0.0)	NR		NR

Note: Data are presented as count (%) or median (interquartile range).

OR was estimated using logistic regression.

Abbreviations: aOR, adjusted OR; CD, cesarean delivery; COVID-19, coronavirus disease 2019; DCOD, Danish COvid-19 in pregnancy database; GA, gestational age; IUFD, intrauterine fetal death; NA, not available; NICU, neonatal intensive care unit; NR, not relevant; OR, odds ratio; SARS,CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Uncomplicated COVID-19 included cases where women did not require admission to hospital due to COVID-19 symptoms and therefore includes women in home isolation or women admitted for obstetrical reasons within 14 days of first positive SARS-CoV-2 test or symptoms.

[b]aOR was adjusted for age, BMI, parity (primi- or multiparity), and smoking.

4 | DISCUSSION

In this prospective population-based cohort study, we found 418 validated cases of SARS-CoV-2 among pregnant women, corresponding to an incidence of 5.1 per 1000 pregnancies. Only 23 women (5.5%) required hospital admission due to the COVID-19 infection. Risk factors for infection were asthma and being foreign born, whereas obesity, smoking, infection after GA 22 weeks, and asthma increased the risk of hospital admission due to COVID-19. We found an increased risk of late termination of pregnancy, but no difference in any delivery or neonatal outcomes among infected women or women with severe infection.

Minority ethnicity has been identified as a risk factor for SARS-CoV-2 infection in both pregnant and non-pregnant women.[2–5,8] The increased risk level found among foreign-born women in this study is similar to that reported in a large systematic review for women of minority ethnicity.[2] The etiology of the disparity is not clear, but it is probably multifaceted and related to cultural and socio-economic factors rather than to SARS-CoV-2.

The identified risk factors for severe infection comprising asthma, obesity, and GA at the time of infection are similar to risk factors identified in previous studies.[2,3] Smoking in pregnancy has not been described previously, but seems a plausible risk factor because of its effect on lung tissue, and smoking women might sooner develop severe respiratory symptoms requiring hospital care. Previous population-based studies have primarily included women admitted to hospital,[3,7,8] and our results in the more severe cases (Table 3) are therefore comparable to the results of these studies.

Women becoming infected after GA 22 weeks had a higher risk of COVID-19-related hospital admission than women becoming infected before 22 weeks. This might indicate an increasing severity of disease with higher GA at infection. However, it may also be explained by a lower threshold to admit women with disease in late pregnancy.

Women with SARS-CoV-2 infection had, as expected, a much higher risk of pneumonia, but otherwise we found no increased risk for adverse maternal or neonatal outcomes in infected compared with non-infected pregnant women. Previous studies have found increased risks of admission to an ICU, induction of labor, preterm delivery, and admission to a NICU,[2–6,20,21] which we could not confirm. The lack of association in our study might be related to the fact that we included all cases of SARS-CoV-2 infection in pregnancy independent of severity. The previously shown associations between SARS-CoV-2 and severe outcomes might be related to severity of disease. We found no statistically significant differences in outcomes among cases requiring hospital admission for COVID-19 compared with less severe cases, but relatively high-risk differences for cesearean section, induction of labor, and admission to a NICU of the neonate. The lack of statistical associations is likely due to low numbers. In a Nordic collaborative study, women with severe COVID-19 were at increased risk of induction of labor cesarean delivery, and preterm delivery.[22] We found few cases of early pregnancy complications among the SARS-CoV-2-infected women. However, after adjustment for exposure time, the risk of termination of pregnancy was higher among the SARS-CoV-2-infected women. In Denmark, all women admitted to hospital are tested for SARS-CoV-2, and we assume that the increased rate of terminations is partly related to more

frequent testing and consequently a higher detection rate of SARS-CoV-2 among women opting for provoked abortion rather than the SARS-CoV-2 diagnosis itself.

This study has several strengths. The major strength is the combination of real-time register-based data considered complete[9] and prospectively collected medical record data, allowing for validation, analysis of disease severity, and multivariate analyses. Furthermore, the comparison population comprised all pregnancies from the same inclusion period as the SARS-CoV-2 cases, thereby adjusting for the possible consequences of community regulations during a pandemic.[23] Additionally, we identified the vast majority of SARS-CoV-2 cases in pregnancy because testing was widespread in Denmark during the inclusion period, and the DCOD data were validated against registry data.

The study also has limitations. First, the register data set was pseudoanonymized, making individual-level linkage to DCOD impossible. Additionally, the data sources of the DCOD and the national registers are different, and the data might not be directly comparable. Nevertheless, the number of SARS-CoV-19 cases was similar in the two cohorts, and data did not differ significantly between the cohorts, indicating agreement between cases and data sources. Some descriptive variables, including BMI and smoking status, are not reported to the registers before delivery and are not reported for early pregnancy losses, causing higher rates of missing data in the registers. Nevertheless, the rates of missing data were similar in the infected and non-infected groups, reducing the risk of bias caused by the missing numbers. Additionally, complete data were available in the DCOD, which also allowed for national surveillance of the infection to support national guidelines until register data were available.[24–26] Second, the lack of association in some outcomes for severe cases might be a result of low numbers. Additionally, the threshold of admitting pregnant women to hospital due to COVID-19 symptoms might be lower than for non-pregnant women, thus diluting the risk estimates of severe disease. Third, universal testing of pregnant women was not implemented in Denmark before May 2020, and we might therefore have missed SARS-CoV-2-positive cases early in the inclusion period. Furthermore, MiBa only included information on PCR tests, so we might have missed pregnant women diagnosed through antigen or antibody tests, which were possibly milder cases. Inclusion of these plausibly positive but non-identified cases in the comparison population of pregnancies might have affected our estimates.

5 | CONCLUSION

In this prospective population-based cohort study with universal SARS-CoV-2 testing, we found no difference in outcomes related to delivery or the neonate among infected women compared with non-infected women. Nor did severity of infection statistically affect the results, but these results have to be interpreted with caution because of low numbers. The results indicate that the outcomes of SARS-CoV-2 infection in pregnancy might not be as severe as proposed by previous studies. The testing strategy and how cases are included naturally influences the results and should be considered.

We found that the incidence of termination of pregnancy among SARS-CoV-2-infected women was increased compared with that in non-infected pregnant women, which might be related to universal screening of women admitted to hospital. Further studies are needed to explore a possible relation between late termination of pregnancy and SARS-CoV-2 infection.

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CONFLICT OF INTERESTS

All authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

AA, LK, MB, LS, KHR, JJ, and LP conceived the registry study, and AA and LK conceived the DCOD study. AA, LK, and MB designed and planned the combined study. AA, MB, TP, and FP acquired and analyzed the data for the cohort study. KW, MI, FJ, ER, CA, IS, TC, JM, LB, BL, AT, MK, BH, LJ, SS, LS, KK, MP, ÅK, MV, DT, MT, LA, AB, AG, CBA, RF, LH, LHv, AS, SR, AA, and LK acquired and managed the DCOD data set and AA analyzed the DCOD data. AA wrote the first draft of the manuscript; MB, LK, TP, LS, KHR, and JJ revised the manuscript critically; and all authors approved the final version of the manuscript.

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REFERENCES

1. World Health Organization. *Rolling updates on coronavirus disease (COVID-19)*. Available online at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen. Accessed August 13, 2020.
2. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320.
3. Vousden N, Bunch K, Morris E, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: a national cohort study using the UK Obstetric Surveillance System (UKOSS). *PLoS One*. 2021;16:e0251123.
4. Overtoom EM, Rosman AN, Swart JJ, et al. SARS-CoV-2 infection in pregnancy during the first wave of COVID-19 in teh Netherlands: a prospective nationwide population-based cohort study. *Authorea*. Published online October 9, 2020. Doi: 10.22541/au.160224307.78021677/v1
5. Jering KS, Claggett BL, Cunningham JW, et al. Clinical characteristics and outcomes of hospitalized women giving birth with and without COVID-19. *JAMA Intern Med*. 2021;181:714-717.
6. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1641-1647.
7. Maraschini A, Corsi E, Salvatore MA, Donati S, ItOSS COVID-19 Working Group. Coronavirus and birth in Italy: results of a national population-based cohort study. *Ann Ist Super Sanita*. 2020;56:378-389.
8. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ*. 2020;369:m2107.
9. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449-490.
10. Voldstedlund M, Haarh M, Mølbak K, MiBa Board of Representatives. The Danish Microbiology Database (MiBa) 2010 to 2013. *Euro Surveill*. 2014;19(19):20667.
11. Pedersen CB, Gøtzsche H, Møller JO, Mortensen PB. The Danish Civil Registration System. A cohort of eight million persons. *Dan Med Bull*. 2006;53:441-449.
12. Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29:541-549.
13. Harritshøj LH, Gybel-Brask M, Afzal S, et al. Comparison of 16 Serological SARS-CoV-2 Immunoassays in 16 Clinical Laboratories. *J Clin Microbiol*. 2021;59:e02596-e2620.
14. Andersen JS, Olivarius NDF, Krasnik A. The Danish National Health Service Register. *Scand J Public Health*. 2011;39:34-37.
15. Bliddal M, Broe A, Pottegård A, Olsen J, Langhoff-Roos J. The Danish Medical Birth Register. *Eur J Epidemiol*. 2018;33:27-36.
16. *The Danish Health and Medicines Authority ("Sundhedsdatastyrelsen"). Digital health solutions*. Available online at: https://sundhedsdatastyrelsen.dk/da/english/digital_health_solutions. Accessed July 20, 2021.
17. *Statistics Denmark*. Available online at: https://statistikbanken.dk/FODIE. Accessed February 4, 2021.
18. Styregruppen for DKN. *Dansk Kvalitetsdatabse for Nyfødte (DKN)*. Datakvalitetsrapport 2019. [Danish Quality Database for Newborns (DKN). Data quality report 2019.] In Danish. Available online at: https://www.sundhed.dk/content/cms/73/102373_dkn_datakvalitetsrapport-2019_offentliggoerelse_04022021.pdf. Accessed February 19, 2021.
19. Vandenbroucke JP, von Elm Erik, Altman DG, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18:805-835.
20. Woodworth KR, Olsen EO, Neelam V, et al. Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy - SET-NET, 16 jurisdictions, March 29-October 14, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1635-1640.
21. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID Multinational Cohort Study. *JAMA Pediatr*. 2021;175:817-826.
22. Engjom H, Aabakke AJ, Klungsøyr K, et al. COVID-19 in pregnancy – characteristics and outcomes of pregnant women admitted to hospital because of SARS-CoV-2 infection in the Nordic countries. *Acta Obstet Gynecol Scand*. 2021. Doi: 10.1111/aogs.14160. Epub ahead of print.
23. Chmielewska B, Barratt I, Townsend R, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021;9:e759-e772.
24. Aabakke AJM, Krebs L. COVID-19 i Graviditet, Rapport for Perioden 1. Marts - 30. August 2020.[COVID-19 in Pregnancy, Report for the Period March 1 - August 30, 2020.] In Danish. Available online at: https://static1.squarespace.com/stahttps://static1.squarespace.com/static/5467abcce4b056d72594db79/t/5f7ef92c2c1737355da5b769/1602156846868/COVID-19+i+graviditet+-+Rapport+for+marts-august+v1.1.pdftic/5467abcce4b056d72594db79/t/5ecfe76495025343e22ccb07/1590683493294/Bilag+F+-+COVID-19+i+graviditet+-+Rapport+for+marts-april+2020_final.pdf. Accessed November 27, 2020.
25. Aabakke AJM, Krebs L. COVID-19 i Graviditet. Rapport for Perioden 1. Marts - 31. Oktober 2020. [COVID-19 in Pregnancy. Report for the Period March 1 - October 31, 2020.] In Danish. Available online at: https://static1.squarespace.com/static/5467abcce4b056d72594db79/t/6046795aaee5296b9de96066/1615231323325/COVID-19+i+graviditet+-+Rapport+for+marts-oktober+v1.1.pdf. Accessed March 23, 2021.
26. Aabakke AJM, Krebs L. COVID-19 i Graviditet. Rapport for Perioden 1. Marts - 30. April 2020. [COVID-19 in Pregnancy. Report for the Period March 1 - April 30, 2020.] In Danish. Available online at: https://static1.squarespace.com/static/5467abcce4b056d72594db79/t/5ecfe76495025343e22ccb07/1590683493294/Bilag+F+-+COVID-19+i+graviditet+-+Rapport+for+marts-april+2020_final.pdf. Accessed March 23, 2021.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

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