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Brief Research Report

Antibody status at delivery and pregnancy outcomes during the first Danish COVID-19 wave

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ABSTRACT

INTRODUCTION. We aimed to investigate the prevalence of SARS-CoV-2 infection and SARS-CoV-2 antibodies in parturient women and their newborns during the first Danish COVID-19 wave and to identify associations with maternal background characteristics, self-reported symptoms, and pregnancy outcomes.

METHODS. In a single-centre, prospective cohort study from Denmark, we invited 1,883 women with singleton pregnancies giving live birth from 25 May 2020 to 2 November 2020. Hereof, 953 (50.6%) women were included. Nasopharyngeal swabs, maternal and umbilical cord blood samples, and questionnaires were collected. Medical records were available for participants and non-participants.

RESULTS. SARS-CoV-2 antibodies were found in 1.3% of the women. All newborns of seropositive women had SARS-CoV-2 antibodies in cord blood. No association was found between SARS-CoV-2 antibodies and pregnancy outcomes. Self-reported loss of smell correlated with seropositivity ($p < 0.001$). No women were hospitalised due to COVID-19 during pregnancy or had a positive nasopharyngeal swab intrapartum.

CONCLUSIONS. The prevalence of COVID-19 in pregnancy was low during the first wave. Maternal SARS-CoV-2 antibodies were associated with antibodies in cord blood, loss of smell and positive SARS-CoV-2 swab during pregnancy, but not with any adverse pregnancy outcomes.

FUNDING. Ferring Pharmaceuticals funded part of the study.

TRIAL REGISTRATION. The study was approved by the Regional Committee on Health Research Ethics (H-20028002) and the Danish Data Protection Agency (P-2020-264).

When planning the present study in March 2020, SARS-CoV-2 was a newly identified virus of unknown epidemiology and impact on pregnancy. The first wave in Denmark developed from February 2020 followed by a second wave starting in October 2020. The infection waves were characterised by new variants, each exerting different influences on pregnancy outcomes. The Delta variant, emerging in April 2021, has been linked to an increased risk of severe maternal adverse outcomes [1, 2].

Prevalence studies on antibody positivity among pregnant women during the first year of COVID-19 have shown varying results across the world with seroprevalence ranging from 1.7% to 11.2% [3-5]. One of these studies (n = 759) reported an increased risk of preterm birth among symptomatic seropositive women [4]. A Danish study with a seroprevalence of 2.6% among 1,313 parturient women found no association between COVID-19 and adverse pregnancy outcomes during the first wave [6].

The objective of this prospective cohort study was to investigate the prevalence of SARS-CoV-2 infection and the presence of antibodies in parturient women and their newborns during the first wave in Denmark. Furthermore, we aimed to identify possible associations with maternal background characteristics, self-reported symptoms, and pregnancy outcomes.

METHODS

The "CareMum COVID-19" study was conducted at the Department of Obstetrics and Gynaecology, Copenhagen University Hospital – North Zealand, Hilleroed; from 25 May 2020 to 2 November 2020. All women with singleton pregnancies giving live birth within the study period (n = 1,883) were invited along with their newborns (**Figure 1**). Maternal blood samples were drawn at admission for delivery and umbilical cord blood samples were obtained immediately after delivery. Total SARS-CoV-2 antibodies (including IgG and IgM) were analysed by a qualitative (positive/negative) assay. The assay has a specificity exceeding 99% and a sensitivity of 95.3% [7]. Only cord samples from newborns of seropositive women were analysed for antibodies. Participating women had a nasopharyngeal swab collected at the time of admission for delivery, which was analysed for SARS-CoV-2 using Reverse Transcription Polymerase Chain Reaction (RT-PCR) as described previously [8]. Participating women completed a questionnaire available in Danish and English about COVID-19 symptoms in 2020. Medical records were available from participants and non-participants. Maternal and neonatal covariates are shown in **Table 1**. Birth weight z-scores were adjusted for gestational age and sex based on Marsal's formula [9].

FIGURE 1 Flow chart of inclusion and sampled data.

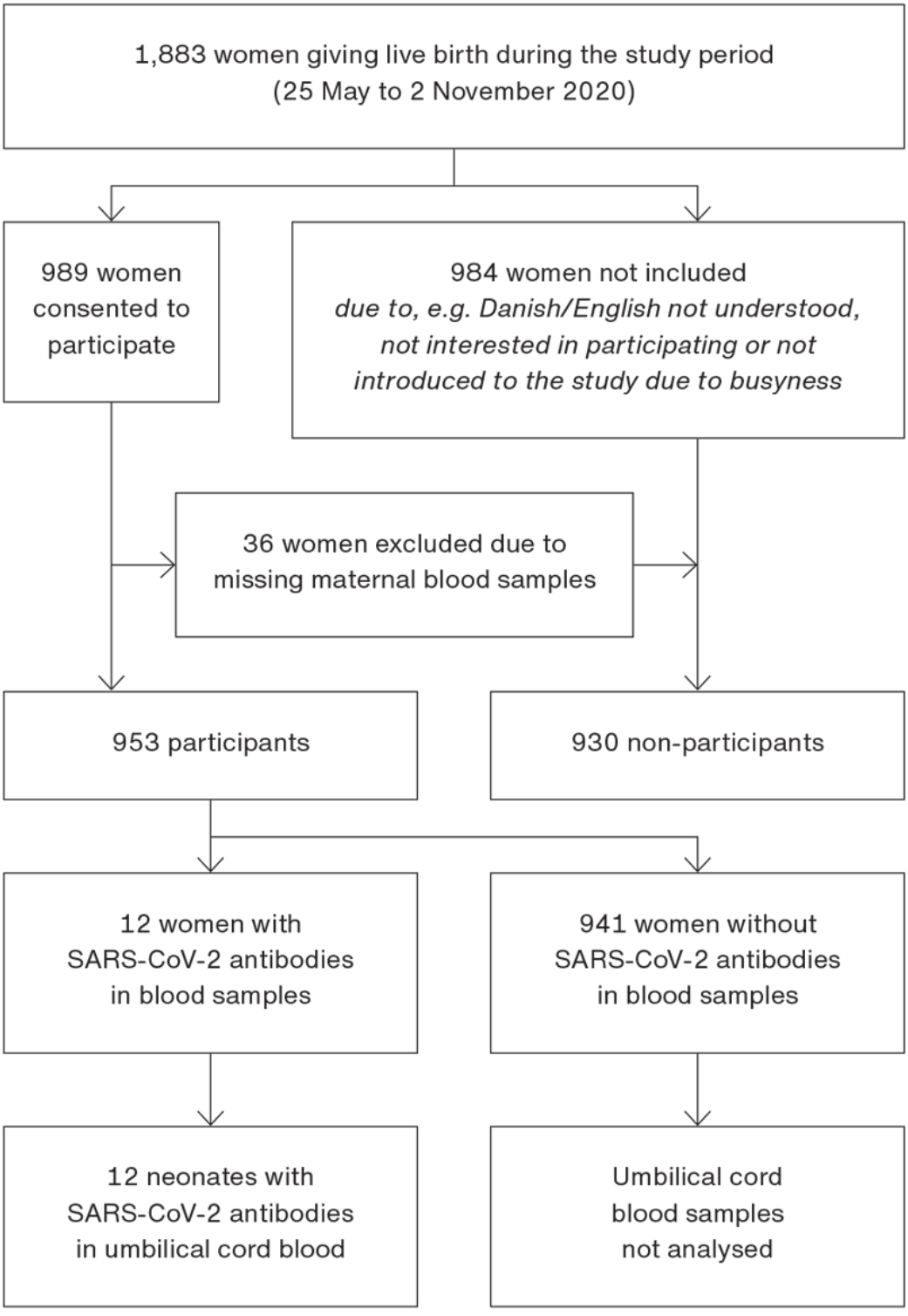

TABLE 1 Maternal background characteristics and pregnancy outcomes by maternal SARS-CoV-2 antibody status (N = 953).

	Women with antibodies (N_w = 12)	Women without antibodies (N_{wo} = 941)	p value
Maternal background characteristics			
Maternal age, mean (± SD), yrs	32.5 (± 5.4)	31.9 (± 4.9)	0.642[e]
Pre-pregnancy BMI, median (25-75%), kg/m²	24.4 (19.1-27.5)	23.5 (21.2-27.0)	0.370[f]
Current smoker or history of smoking, % (n/N)	16.7 (2/12)	24.3 (228/938)[h]	0.741[g]
Nulliparous, % (n/N)	16.7 (2/12)	37.3 (351/941)	0.228[g]
Danish ethnicity, % (n/N)	83.3 (10/12)	84.4 (771/913)[h]	> 0.999[g]
Cohabiting with partner, % (n/N)	100 (11/11)[h]	96.8 (905/935)[h]	> 0.999[g]
Pre-existing medical condition, % (n/N):			
Respiratory-related conditions[a]	16.7 (2/12)	6.9 (65/941)	0.204[g]
Other medical conditions[b]	8.3 (1/12)	29.1 (274/941)	0.196[g]
Positive SARS-CoV-2 nasopharyngeal swab, % (n/N):			
During pregnancy	33.3 (4/12)	0.1 (1/938)[h]	< 0.001[g]
At time of admission for delivery	0.0 (0/12)	0.0 (0/941)	-
COVID-19-suspected symptoms during 2020, % (n/N)[c]:			
Loss of smell	58.3 (7/12)	7.8 (73/941)	< 0.001[g]
Other symptoms	83.3 (10/12)	70.6 (664/941)	0.525[g]
Pregnancy outcomes			
Pregnancy complications, % (n/N):			
Hypertensive disorders in pregnancy[d]	0.0 (0/12)	7.0 (66/941)	> 0.999[g]
Gestational diabetes mellitus	0.0 (0/12)	4.3 (40/941)	> 0.999[g]
Cholestasis in pregnancy	8.3 (1/12)	1.5 (14/941)	0.174[g]
Maternal admission due to COVID-19, % (n/N)	0.0 (0/12)	0.0 (0/941)	-
Obstetric outcomes, % (n/N):			
Induced labour	8.3 (1/12)	30.2 (284/941)	0.122[g]
Vaginal delivery	91.7 (11/12)	76.6 (721/941)	0.314[g]
Acute Caesarean delivery	0.0 (0/12)	12.5 (118/941)	0.380[g]
Elective caesarean delivery	8.3 (1/12)	10.8 (102/941)	> 0.999[g]
Neonatal outcomes:			
Gestational age, median (25-75%), days	279.5 (273.8-284.0)	282.0 (273.0-287.0)	0.412[f]
Preterm delivery: < 37+0 wks, % (n/N)	8.3 (1/12)	2.7 (25/941)	0.284[g]
Female sex, % (n/N)	58.3 (7/12)	43.8 (412/941)	0.385[g]
Birth weight, mean (± SD), Z-score	-0.24 (± 0.8)	0.05 (± 1.1)	0.315[e]
Arterial pH < 7.1 in cord blood, % (n/N)	0.0 (0/12)	0.4 (4/941)	> 0.999[g]
NICU, % (n/N)	0.0 (0/12)	9.4 (82/941)	0.614[g]

HELLP = haemolysis, elevated liver enzymes, low platelet count; NICU = neonatal intensive care unit; SD = standard deviation.
a) Included women with a diagnosis of respiratory disease or with prescribed inhalation medication.
b) Combined and included psychological disorders (e.g. anxiety, ADHD, and depression), thyroid, gastrointestinal, rheumatoid, neurological, and gynaecological diseases.
c) Self-reported symptoms during 2020 sub-grouped into loss of smell and other symptoms: fever, cough, sore throat, headache, muscle soreness, shortness of breath, nasal congestion, and diarrhoea.
d) Defined by gestational hypertension, preeclampsia or HELLP.
e) Student's T-test.
f) Mann-Whitney test.
g) Fisher's exact test.
h) Total numbers are divergent due to missing data.

Statistical analyses

Data were analysed using IBM SPSS version 27.

Ethics

All participants provided oral and written informed consent. Caretakers holding parental authority provided informed consent on behalf of their newborn.

Trial registration: The study was approved by the Regional Committee on Health Research Ethics (H-20028002) and the Danish Data Protection Agency (P-2020-264).

RESULTS

This study included 953 (50.6% of the eligible women) mother-newborn pairs. No women tested positive for SARS-CoV-2 intrapartum. SARS-CoV-2 antibodies were found in 12 women (1.3%). All newborns from seropositive women had SARS-CoV-2 antibodies in cord blood. Significantly more women with than without SARS-CoV-2 antibodies tested positive by a nasopharyngeal swab during pregnancy (33.3% versus 0.1%, $p < 0.001$). In addition, significantly more women with SARS-CoV-2 antibodies reported loss of smell during 2020 (58.3% versus 7.8%, $p < 0.001$). No other demographic or clinical background data differed between the two groups. No significant differences were recorded in pregnancy outcomes between the two groups.

Participants were significantly older than non-participants, were more often of Danish ethnicity and were more often cohabiting with a partner (Supplementary Table). More participants had hypertensive disorders of pregnancy, induced labour and elective Caesarean delivery. No differences were registered in neonatal outcomes between the two groups, besides more newborns of female sex being born to non-participants ($p = 0.004$).

DISCUSSION

This study found a 1.3% SARS-CoV-2 antibody prevalence in parturient women during the first COVID-19 wave in Denmark. Self-reported loss of smell and positive SARS-CoV-2 nasopharyngeal swab during pregnancy were associated with maternal antibodies. SARS-CoV-2 antibodies were detected in all umbilical cord blood samples from newborns of seropositive women, which corresponded well with the antibody transfer rate shown in other studies [10].

The prospective cohort design and inclusion of data from non-participants are strengths of the present study, providing estimates of the prevalence and clinical consequences of SARS-CoV-2 infection among parturient women during the first COVID-19 wave, which was characterised by a low testing capacity.

Our study is, however, limited by lack of power due to the low prevalence of SARS-CoV-2 infection during the study period, an unknown factor during the planning of the study. Consequently, firm

conclusions regarding adverse pregnancy outcomes cannot be drawn from the present study.

Comparing our study to a Danish cohort by Egerup et al. from Copenhagen [6], we found a lower SARS-CoV-2 antibody prevalence (1.3% versus 2.1%). Other studies among pregnant women found a prevalence of 1.7% in Norway; 6.2% in Philadelphia, United States; and 11.2% in Spain [3-5]. Risk factors for infection include age, healthcare work, low economic status, and multi-generational households [11, 12]. Studies among pregnant women found that being foreign born or of non-white ethnicity was a risk factor for infection [13, 14]. Egerup et al. did not report on ethnicity or characteristics of non-participants. Therefore, the observed difference in seroprevalence between the two cohorts is most likely multifactorial including cultural, demographic, and socio-economic factors. Furthermore, our study was limited by inclusion of only Danish or English-speaking women with more women of Danish ethnicity among participants than non-participants. Therefore, selection bias may have caused a lower prevalence of SARS-CoV-2 than that found by Egerup et al. from another part of the Capital Region of Denmark.

Consistent with findings from other studies, our study showed that the self-reported symptom "loss of smell" was associated with seropositivity [11, 12].

We found no association between SARS-CoV-2 antibodies and pregnancy outcomes, which is supported by other Danish studies from the same period [6, 13]. However, a nationwide cohort study covering the first and second Danish waves found that women infected with SARS-CoV-2 during pregnancy were at increased risk of hypertensive disorders in pregnancy and preterm delivery [15]. A Dutch study found an increased risk of Caesarean section, hospital and intensive care unit admission when infected with SARS-CoV-2 [16], and a Spanish study reported an increased risk of preterm birth and Caesarean delivery among symptomatic seropositive women [4]. None of these associations were found in our study.

CONCLUSIONS

In this prospective cohort study of parturient women during the first COVID-19 wave in Denmark, we found no cases of SARS-CoV-2 infection intrapartum. The prevalence of SARS-CoV-2 antibodies was low, and all newborns of seropositive women had antibodies in cord blood. Self-reported loss of smell and positive nasopharyngeal swab during pregnancy was associated with maternal antibodies. Neither maternal nor cord blood antibodies were associated with adverse pregnancy outcomes.

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Conflicts of interest none. Disclosure forms provided by the authors are available with the article at

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Supplementary Material https://content.ugeskriftet.dk/sites/default/files/2024-04/a10230657-supplementary.pdf

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