Title: SARS-CoV-2 infection in pregnancy during the first wave of COVID-19 in the Netherlands: a prospective nationwide population-based cohort study

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Running title: SARS-CoV-2 infection in pregnant women in the Netherlands

Abstract

Objective: Description of characteristics, risk factors, management strategies and maternal, obstetric and neonatal outcomes of SARS-CoV-2 infected pregnant women in the Netherlands.

Design: Multi-centre prospective nationwide population-based cohort study.

Setting: Nationwide.

Population: All pregnant women in the Netherlands with confirmed SARS-CoV-2 infection in home-isolation or admitted to hospital between March 1st, 2020 and August 31st, 2020.

Methods: Pregnant women with positive PCR or antibody tests were registered using the Netherlands Obstetrics Surveillance System. Testing occurred according to national guidelines (selective testing). Data from the national birth registry (Perined) and Dutch National Institute for Public Health and the Environment (RIVM) were used as reference.

Main Outcome Measures: Incidence of pregnant women with SARS-CoV-2 infection. Maternal, obstetric and neonatal outcomes including hospital and critical care admission, clinical management and mode of birth.

Results: Of 312 registered women, 65 (20%) were admitted to hospital, of whom 5 (2%) to intensive care and 9 (14%) to obstetric high care units. Risk factors for admission were non-Caucasian background (n=28; OR 6.67, 95%CI 4.08-10.90) and being overweight or obese (n=38; OR 2.64, 95%CI1.51 to 4.61). Hospital and intensive care admission were higher compared to age-matched infected women (respectively, OR 14.57, 95%CI 10.99-19.03 and OR 5.02, 95%CI 2.04-12.34). One maternal death occurred. Caesarean section after labour onset was increased (OR 2.50; 95%CI 1.57-3.97).

Conclusions: Pregnant women with SARS-CoV-2 infection are at increased risk of hospital admission, ICU admission and caesarean section.

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Keywords: Pregnancy, COVID-19, SARS-CoV-2, Pregnancy complications, Pregnancy outcome, Obstetric surveillance system.

Tweetable abstract: Pregnant women with SARS-CoV-2 in the Netherlands show increased hospital/ICU admission and caesarean section.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic resulting from the novel coronavirus SARS-CoV-2, has a major impact worldwide.(1) High-risk populations have been identified, including the elderly, obese and black or specific ethnic minority groups. Evidence is now increasing that pregnant women and their unborn children may also comprise a vulnerable group, with higher rates of intensive care (ICU) admission and mechanical ventilation.(2, 3)

Previous studies have shown that not only are pregnant women more frequently affected by pneumonia arising from any infectious aetiology, but their outcomes are often worse compared to the non-pregnant population.(4) The maternal physiological adaptations taking place in pregnancy (e.g., diaphragm elevation, increased oxygen consumption, oedema of respiratory tract mucosa and increased clotting tendency) as well as the physiological state of relative immune suppression in pregnancy place pregnant women at increased risk of poor outcomes, and it is likely that these mechanisms will also play a role in COVID-19.(5) During the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, risks of maternal mortality and severe morbidity, as well as miscarriages and preterm labour were considerable.(5)

Initial knowledge on pregnancy and SARS-CoV-2 was based on facility-based case reports and small case series.(6) A recent meta-analysis, including a mixed group of studies with different testing policies and selected groups of infected women, indicates that pregnant women may be at increased risk of ICU admission compared with age-matched non pregnant women. Rates of vertical transmission appear to be very low.(7) In a population-based cohort of 427 pregnant women with SARS-CoV-2 admitted to hospital in the UK, there were disproportionally large proportions of black, Asian and ethnic minority women, obese women and women with pre-existing conditions.(8) Since most studies to date have only

reported on women admitted to hospital, it is unclear whether risk of hospital admission itself is increased among pregnant women, and whether findings in terms of risk groups can be generalised to all pregnant women with COVID-19.

In this present study, we have collected information on all pregnant women with a confirmed SARS-CoV-2 infection in the Netherlands, whether they were admitted to hospital or in home-isolation. The primary aim of this study was to evaluate the severity of SARS-CoV-2 infection in pregnant women and their newborns, compared to non-pregnant women in the same age group.

Method

This is a multi-centre prospective nationwide population-based cohort study conducted between March 1st, 2020 and August 31st, 2020 in the Netherlands. Cases were ascertained using the Netherlands Obstetric Surveillance System (NethOSS), a nationwide registration system functioning under the umbrella of the Dutch Birth Registry (Perined), in which maternal mortality, severe maternal morbidity and rare diseases in pregnancy are registered. (9, 10) All hospitals in the Netherlands with an obstetrician-led maternity unit (N=74) were asked to report pregnant or postpartum women up to 42 days with a confirmed SARS-CoV-2 infection to the NethOSS. All midwifery practices (N=577) in the Netherlands were approached through the Society of Midwifery (KNOV), maternity care ('BO geboortezorg') and the Dutch Perinatal Registry (Perined) and were also asked to report. From March 2020, the joint national guideline on SARS-CoV-2 infection in pregnancy of the Dutch Society of Obstetrics and Gynaecology (NVOG), the Royal Society of Midwifery (KNOV) and maternity care ('BO geboortezorg'), Dutch Society of Paediatricians (NVK) and the Dutch National Institute for Public Health and the Environment (RIVM) included that all confirmed cases had to be reported to the NethOSS.

In each hospital in the Netherlands with an obstetrician-led maternity unit (N=74) a NethOSS reporting clinician was nominated to report cases and asked to communicate this within the perinatal cooperation group. Weekly requests were sent through email to the aforementioned clinicians in each hospital. This email contained a reporting link specific to each individual reporter. Clinicians were asked to report any case meeting the inclusion criteria or to reply with '0' if they had no cases to report in order to ascertain validity. When a positive case was reported, reporting clinicians were asked to provide additional information with regard to year of birth, parity, estimated date of birth, date of positive SARS-CoV-2 test and information on hospital admission, pharmacological treatment and/or oxygen supplementation and whether she had given birth. Subsequently, a data collection form with additional questions was sent to each clinician. Case report forms of women reported by midwifery practices were filled out

by the reporting midwives. The data collection form was designed by the INOSS (International Network of Obstetric Survey Systems), based on the UKOSS form with input from the World Health Organisation (WHO) and slightly adapted to the Dutch health care system.(11)

For nationwide comparison, a control group of pregnant women was established with information from the Dutch Perinatal Registry (Perined). This registry contains population-based information pertaining to 99% of pregnancies in the Netherlands.(12) Specific information of all women in the registry who had given birth between March 1st, 2017 and March 1st, 2018, the most recent year with complete data, was used as reference. For comparison with non-pregnant women in the fertile age group, hospital and ICU admissions among women were obtained from the National Institute for Public Health and the Environment (RIVM) and the National Intensive Care Evaluation (NICE). All women, pregnant and non-pregnant, between 20 and 50 years with positive SARS-CoV-2 in PCR or by imaging registered until September 22nd, 2020 were included in the reference group.

As a result of limited testing capacity, the testing policy in the Netherlands from March 12th, 2020 focused on severely ill people with a suspected SARS-CoV-2 infection, high-risk groups and healthcare staff working during the COVID-19 pandemic. High risk groups were people with an increased risk of severe illness from SARS-CoV-2. Pregnant women were at that time not considered as a high-risk group.(13) Between March 12th, 2020 and April 30th, 2020, policy by the Dutch National Institute for Public Health and the Environment (RIVM) stated that pregnant women required testing only in case of serious complaints or if hospital admission due to SARS-CoV-2 related complaints was required. Testing capacity was slowly expanded in April and from April 30th, 2020 all people were asked to test if they had symptoms related to SARS-CoV-2 infection for longer than 24 hours. The two available tests in the Netherlands were polymerase chain reaction (PCR) using samples taken from the

nose and throat with a cotton swab or a serological test based on the presence of SARS-CoV-2 specific antibodies.

The outcomes collected were signs of pneumonia on imaging, hospital admission, (N)ICU or obstetric high care admission and administration of pharmacological therapy. We recorded characteristics of women such as body mass index (BMI), age, ethnicity, comorbidities and gestational age at onset of symptoms. For women who had given birth, mode of birth, induction, analgesia, intrauterine or peripartum transmission and breastfeeding were assessed. Admission to hospital was defined by hospital stay for longer than 24 hours and for non-obstetric reasons. Women admitted for delivery only were not included. Women at birth were divided in a symptomatic and asymptomatic group. Women were considered symptomatic at birth if complaints related to SARS-CoV-2 infection were reported at the start of birth. The incidence of SARS-CoV-2 infection was estimated using the most recently available data from the Dutch Perinatal Registry (Perined). In 2018, 79 962 pregnancies were reported in six months.

Ethnicity was defined by country of origin based on the definition of Statistics Netherlands. If the woman was born in the Netherlands with at least one of her parents born abroad, she was considered to be from the same origin as her parent(s) from outside the country. Body mass index (BMI) was defined according to the first recorded weight in pregnancy up to 12 weeks. A woman was considered overweight with BMI above 25 and obese with BMI above 30. Gestational age was based on first trimester dating ultrasound.

Statistical analyses were carried out using IBM SPSS 25 (SPSS Inc., Chicago, IL, USA). Descriptive analyses were performed. Proportions are presented as percentages, skewed distributions as medians with ranges. For categorical data, differences are presented as odds ratio (OR) with 95% confidence intervals (95% CI).

Results

Between March 1st, 2020 and August 31st, 2020, a total of 330 SARS-CoV-2 positive women were registered. In 18 women, a positive test result was reported, but additional information could not be retrieved. Additional data were returned for 312 cases (95%). The estimated incidence of SARS-CoV-2 among pregnant women in the Netherlands over these six months was 4.13 per 1000 maternities. Estimated incidence was highest during the first three months of registration (March to May) with 5.90 per 1000 maternities. The number of positive cases per week can be seen in figure 1 *(Supporting Information)*. Of all reported cases, 172 women were still pregnant, while 139 had given birth by September 22nd, 2020. The majority of women registered were not admitted to hospital (N=208, 67%). Instead they stayed, as advised by the Dutch government, in home isolation until two weeks after their complaints had subsided.

One case of maternal mortality (0.3%) was reported. This concerned a non-Caucasian woman who tested positive at term and consequently was induced. She gave birth via caesarean section because of previous caesarean section and prolonged labour and was admitted to ICU 3 days after giving birth. She died after 27 days in ICU due to complications caused by SARS-CoV-2 infection. An overview of background characteristics is shown in table 1. In table 2 women are divided in two groups: home isolation and hospital admission. Among women testing positive for SARS-CoV-2, ethnic minorities were disproportionately present in comparison to the general population of pregnant women in the Netherlands (N=93, 37%; OR 3.46, 95%CI 2.72-4.40) and particularly among women admitted to hospital (N=28, 48%; OR 6.67, 95%CI 4.08-10.90). Overweight and obese women represented a large proportion of women with SARS-CoV-2 infection (N=124, 50%) and overweight and obese women were more often admitted to hospital (OR 2.64, 95%CI 1.51-4.61) compared to women with a normal BMI.

Sixty-five (21%) women were admitted to hospital and five women required ICU treatment, which represents 8% of women admitted to hospital and 2% of all registered women. Another nine women (14%) were admitted to high obstetric care units with additional monitoring facilities but did not require mechanical ventilation. Compared to 41 851 women aged 20-50 who tested positive for SARS-CoV-2 in the Netherlands, of whom 693 (1.7%) were admitted to hospital and 118 (0,3%) to ICU, ORs for hospital and ICU admission were considerably increased among pregnant women: OR 14.57, 95%CI 10.99-19.03 and OR 5.02, 95%CI 2.04-12.34 respectively. Of the pregnant women that required ICU admission, two were admitted antepartum and three postpartum. One woman had a caesarean section while still on mechanical ventilation.

In 34 women (13%) signs of pneumonia were found on imaging. Women most frequently complained of cough (N= 146, 56%), breathlessness (N=81, 31%) and flu-like symptoms (N=77, 30%) and 123 women (47%) had a fever. Antibiotics were administered in 39 women (16%), the type of antibiotic varied. In three women (1%) antiviral drugs were prescribed (oseltamivir, N=2, remdesivir, N=1). In eleven women (4%), corticosteroids were administered to stimulate fetal lung maturation. In five of these women this was due to signs of threatening preterm labour, while in six others the risk of iatrogenic preterm labour was considered high due to the severity of COVID-19. Oxygen supplementation was used in 28 women (11%) with signs of breathlessness and low oxygen levels measured using a pulse oximeter (SpO2). Three women (1%) needed mechanical ventilation of whom two were ventilated in a prone position.

Four women had a miscarriage, of whom two a late miscarriage after 12 weeks' gestation and one woman was diagnosed with a molar pregnancy, managed by suction curettage.

Specifics with regard to the 139 women (42%) who had given birth are provided in Table 3. Out of 139 women, 48 (36%) were symptomatic at birth. Compared with the reference group,

the risk of caesarean section was increased (OR 1.91, 95%CI 1.29-2.83). Pre-labour caesarean section was performed in 12 women (10%). In only one woman the indication was COVID-related, the other 11 had various obstetric indications such as breech presentation or previous caesarean section. Reasons for caesarean section during birth (N=21, 17%) were obstructed labour (N=12, 57%) suspected fetal distress (N=7, 33%), a combination of obstructed labour and suspected fetal distress (N=1, 5%) maternal request after onset of labour with previous caesarean section (5%), or unknown (N=1, 5%). Risk of caesarean section was most evident in women with SARS-CoV-2 related symptoms at birth, compared with the reference group (N=18, OR 2.63, 95%CI 1.52-4.57). The risk of caesarean section was not significant for women asymptomatic at birth compared with the reference group (N=15, OR 1.44, 95%CI 0.82-2.53). Labour was induced in 63 women (50%), of whom in 16 (25%) due to COVID-19.

An overview of neonatal results can be found in table 4. No cases of vertical transmission or neonatal death were reported. There were three twin pregnancies, resulting in 137 live births. Of these, 22 neonates were admitted to a neonatal unit (7%), 14 were born preterm and five before 34 weeks' gestation. Three neonates were admitted due to suspicion of infection.

Discussion

Main findings

This large nationwide population-based registration study (NethOSS) has provided the outcomes of pregnant and postpartum women in the Netherlands who had been infected with SARS-CoV-2, during the first wave up to August 31st, 2020. Our findings indicate that pregnant women with SARS-CoV-2 in the Netherlands were at higher risk of hospital admission, especially obstetric high care and ICU. One case of maternal mortality was reported. Most women admitted to hospital were in the third trimester. Among women admitted in hospital compared to home isolation, those who were overweight and from non-Caucasian backgrounds were overrepresented. Labour induction and opiate use during labour were more common among women with SARS-CoV-2 and these women had a higher risk of caesarean section compared with pregnant women without SARS-CoV-2 infection. The risk of preterm birth was not elevated. No case of vertical transmission was reported

Strengths and limitations

The prospective population-based study design with participation of all Dutch hospitals with an obstetrician-led maternity unit as well as all midwifery practices and the comparison with data from national perinatal registry are strengths of the current study. We applied the NethOSS registration system that has been in use for nationwide registration of maternal mortality and severe maternal morbidity since 2013. This has resulted in a high case ascertainment. The Dutch National Institute for Public Health and the Environment (RIVM) stopped reporting the number of pregnant women positive for SARS-CoV-2 from April 2nd, 2020. They had reported 78 cases by that date, compared with 98 cases reported to NethOSS.(14) Our results included women with pregnancies of all gestational ages and women admitted to hospital and in home-isolation with no or mild complaints.

Our study has several limitations. As a result of testing policies in the Netherlands, tests initially were limited to people with significant symptoms requiring hospital admission (from March 12th to April 30th, 2020). Therefore, not all pregnant and postpartum women were tested, and some underreporting of COVID-19 infections is probable. Testing was expanded from May 1st, which is likely to have resulted in more women with mild or no symptoms being included in our study. The now ongoing second wave with more liberal testing policy will only solve this problem partially. To our knowledge there is no other study reporting on SARS-CoV-2 infection in pregnancy where the whole pregnant population is tested on a regular base.

There may have been some underreporting of infections in women attending community midwives, since these women were indirectly registered through the reporting hospital clinician. To minimize the number of missing cases, midwifery practices were actively involved in the registration process through different communication channels.

Registration is still ongoing, and many women analysed in this report are still pregnant, at the time of writing (N=191). The effect of SARS-CoV-2 on pregnancy, birth and newborns could therefore not be assessed completely for this group. At present a second wave started, it will be interesting to analyse the perinatal outcomes in the pregnant women also in women who have been infected in the first and second trimester, since these data are scarce.(7)

Interpretation

Even though the majority of pregnant women with SARS-CoV-2 infection experienced mild symptoms, a small but significant group developed severe morbidity. When comparing these results to those of women in the same age group, pregnant women were more often admitted to hospital and ICU. The reference group contained women until 50. Since risk of hospital admission is reported to increase with age and pregnant women in our study population above 40 were scarce (8%) and above 45 absent, we assume that the risk could

be even higher when compared with women until 40.(15) This is the first study increased risk of hospital admission in Sars-CoV-2 infected pregnant women in comparison to age matched infected non pregnant women. Increased ICU admission is supported by recent evidence.(7, 16)

Incidence of SARS-CoV-2 infection among pregnant women in the Netherlands was slightly higher than reported for the United Kingdom, but the UK sample was limited to women admitted to hospital, rendering comparisons only possible after IPD meta-analysis. It is very likely that the incidence of all infections was much higher in the UK, as reflected in the general population.(17) Most other reported studies are facility-based.(8, 18) The population-based registration studies into SARS-COV-2 in pregnancy performed so far are all from members of the International Obstetric Survey System Network (INOSS). The United Kingdom Obstetric Surveillance System (UKOSS), Italian Obstetric Surveillance System (ItOSS) and NethOSS used the same study protocol, design (uniform definitions, data collection methods and collected variables) and a similar case report form. The UKOSS showed a similar rate of ICU admission and higher risk of hospital admission for women from black or other ethnic minority groups, overweight or obese women, as well as older age and pre-existing comorbidities.(19-21)

An increased risk of caesarean section was demonstrated in the group of SARS-CoV-2 infected women (OR1.91, 95%CI 1.29-2.83), especially when they had SARS-CoV-2 related symptoms at birth (OR2.63 (1.62-4.57). Similar increases have been reported in the United Kingdom, Italy and New York City.(8, 18, 22) This might be due to increased caution of the attending physician or the presence of specific background characteristics such as high BMI and pre-existing disease, which increase the risk of both SARS-CoV-2 infection and caesarean section. The neonatal outcomes in our study were reassuring and similar to results in other studies.(7)

To guide therapy and vaccination policies in the vulnerable group of pregnant women, especially the subgroups at risk of severe disease, international IPD meta-analysis based on

326 robust population-based data is warranted within INOSS, where in 17 countries uniform data
327 on hospital admitted SARS-CoV-2 positive pregnant women were collected. Long-term
328 consequences of SARS-CoV-2 infection for women and their babies remain unknown and
329 are also urgently needed. (23-27)

Conclusions

It is increasingly clear that pregnant women may also comprise a vulnerable group in the COVID-19 pandemic. In the Netherlands, pregnant and postpartum women infected with SARS-CoV-2 appear to be at higher risk of hospital and ICU admission compared to other women in the same age group. Non-Caucasian background and being overweight or obese were risk factors for hospital admission. The influence of infection on maternal complications seems highest during the third trimester. Infected women had higher odds of being induced or giving birth by caesarean section. Pregnant women should therefore be advised to adhere to social distancing and early testing and registration should be facilitated. Moreover, pregnant women with SARS-CoV-2 infection should be closely monitored, particularly in presence of additional risk factors and long term follow up studies are warranted.

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Disclosure of Interest

The authors report no conflict of interest.

Contribution to Authorship

EO and KB designed the study. EO wrote the first draft of the manuscript. EO and AR did the analyses. EO, AR, JZ, TS, TvdA and KB contributed to the development and conduct of the study. EO, AR, JZ, TV, TS, TvdaA and KB contributed to interpretation of data edited and approved the final version of the article.

Details of ethical approval

All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The NethOSS registration system is part of the National Perinatal Registry foundation in the Netherlands (Perined). This study did not require specific ethical approval and Informed consent of participants was not obtained since Perined is allowed administrative permission in the Netherlands in order to access patient information from patient charts if the information used is not personally identifiable, concerns large numbers of participants and it is not feasible to trace and contact individual participants.

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Table 1: Background characteristics: pregnant women with SARS-CoV-2 versus reference group

Characteristics	Pregnant women with SARS-CoV-2 N=312 n (%)	Reference group of pregnant women* N=183,413 n (%)	OR (95% CI)[1] Pregnant women with SARS-CoV-2 versus reference group
General			
Age			
<25	19 (6)	16,662 (9)	**0.61 (0.39-0.97)**
25-30	74 (24)	54,837 (30)	**0.68 (0.52-0.88)**
30-35	131 (43)	70,615 (39)	1.05 (0.84-1.31)
35-40	61 (20)	34,290 (19)	0.99 (0.75-1.30)
>40	23 (8)	6,913 (4)	**1.91 (1.25-2.92)**
Missing	*4*	*86*	
Ethnicity			
Caucasian	158 (63)	161,464 (88)	**0.13 (0.10-0.16)**
Turkish	12 (5)	6 (0)	
African	50 (20)	5 (0)	
Asian	15 (6)	7,401 (4)	1.13 (0.67-1.90)
Latin American	4 (2)	4,681 (3)	0.47 (0.18-1.26)
Other	12 (5)	6,593 (4)	1.01 (0.57-1.80)
Missing	*61*	*3,261 (2)*	
BMI			
Normal (<25)	125 (51)	na	
Overweight (25-30)	73 (29)	na	
Obese >30	51 (21)	na	
Missing	*63*		
Smoking			
Current	14 (5)	na	
Missing	*53*	*na*	
Pre-existing medical problems			
Pulmonary disease	15 (6)	na	
Cardiac disease	6 (2)	na	
Diabetes	6 (2)	na	
Pregnancy			
Parity			
Nulliparous	132 (43)	79,518 (43)	0.87 (0.70-1.09)
Multiparous	175 (57)	103,549 (56)	0.87 (0.70-1.08)
Missing	*5*	336	
Gestational age at positive test			
<22	88 (30)	N/A	
22-27	57 (19)	N/A	
28-31	31 (10)	N/A	
32-36	51 (17)	N/A	
37 or more	55 (19)	N/A	
Postpartum	16 (5)	N/A	
Missing	*14*		
Multiple pregnancy	6 (2)	5.270 (3)	0.63 (0.28-1.42)
Signs of premature labour	11 (4)	4.226 (2)	1.46 (0.80-2.67)

* Reference group from pregnant women in the Dutch Perinatal Registry (Perined) between March 1st 2017 – march 1st 2018

*Odds Ratio between pregnant women with SARS-CoV-2 who have given birth and reference group from Dutch Perinatal Registry

na = not available

Table 2: Background characteristics: women in home isolation compared with women admitted to hospital

Characteristics	Women in home isolation N=247 n (%)	Women admitted to hospital N=65 n (%)	OR (95% CI)* Hospital admission versus home isolation
General			
Age			
<25	15 (6)	4 (6)	1.01 (0.33-3.17)
25-30	63 (26)	11 (17)	0.60 (0.29-1.21)
30-35	99 (41)	32 (49)	1.45 (0.84-2.51)
35-40	49 (20)	12 (19)	0.92 (0.45-1.84)
>40	17 (7)	6 (9)	1.38 (0.52-3.64)
Missing	*4*	*0*	
Ethnicity			
Caucasian	128 (66)	30 (52)	0.80 (0.46-1.38)
Turkish	7 (4)	5 (9)	2.86 (0.88-9.32)
African	34 (18)	16 (28)	**2.05 (1.05-4.00)**
Asian	11 (6)	4 (7)	1.41 (0.43-4.57)
Latin American	2 (1)	2 (3)	3.89 (0.54-28.15)
Other	11 (6)	1 (2)	0.34 (0.04-2.65)
Missing	*54*	*7*	
BMI			
Normal (<25)	103 (55)	22 (37)	0.72 (0.40-1.27)
Overweight (25-30)	52 (28)	21 (35)	1.79 (0.98-3.27)
Obese >30	34 (18)	17 (28)	**2.22 (1.15-4.30)**
Missing	*58*	*5*	
Smoking			
Current	7 (4)	7 (11)	2.86 (0.88-9.32)
Missing	*51*	*2*	
Pre-existing medical problems			
Pulmonary disease	9 (5)	6 (10)	2.69 (0.92-7.85)
Cardiac disease	4 (2)	2 (3)	1.93 (0.35-10.77)
Diabetes	5 (2)	1 (2)	0.76 (0.09-6.59)
Pregnancy			
Parity			
Nulliparous	104 (43)	28 (43)	1.04 (0.60-1.81)
Multiparous	138 (57)	37 (57)	1.04 (0.60-1.81)
Missing	*5*	*0*	
Gestational age at positive test			
<22	79 (34)	9 (14)	**0.34 (0.16-0.73)**
22-27	45 (19)	12 (19)	1.02 (0.50-2.06)
28-31	22 (9)	9 (14)	1.64 (0.72-3.77)
32-36	38 (16)	13 (20)	1.38 (0.68-2.77)
37 or more	44 (19)	11 (17)	0.94 (0.46-1.94)
Postpartum	5 (2)	11 (17)	**9.86 (3.29-29.55)**
Missing	*14*	*0*	
Multiple pregnancy	5 (3)	1 (2)	0.76 (0.09-6.59)
Signs of premature labour	4 (2)	7 (11)	**7.33 (2.08-25.89)**

*Odds Ratio between pregnant women with SARS-CoV-2 in home isolation and pregnant women with SARS-CoV-2 admitted to hospital

460 **Table 3: Birth characteristics**

	Women with SARS-CoV-2 who have given birth **N=139** **n (%)**	**Reference group of women who have given birth*** **N=183,413** **n (%)**	**OR (95% CI)**** Pregnant women with SARS-CoV-2 compared with reference group	**Women with SARS-CoV-2 who were symptomatic at birth** **N=60** **n (%)**	**OR (95% CI)***** Pregnant women with SARS-CoV-2 who were symptomatic compared with reference group
Mode of birth:					
Vaginal birth	85 (68)	123,709 (76)	0.76 (0.54-1.07)	33 (60)	**0.59 (0.35-0.98)**
Instrumental vaginal birth	7 (6)	12,802 (8)	0.71 (0.33-1.51)	4 (7)	0.95 (0.35-2.63)
Pre-labour caesarean section	12 (10)	13,477 (8)	1.19 (0.66 -.,15)	6 (11)	1.40 (0.60-3.26)
Caesarean section after onset of labour	21 (17)	12,203 (8)	**2.50 (1.57-3.97)**	12 (22)	**3.51 (1.86-6.61)**
Missing	*14*	*21,214*		*5*	
Gestational age at birth					
16+0 - <36+6	15 (12)	12,352 (10)	1.68 (0.98-1,86)	8 (15)	**2.13 (1.01-4.49)**
37-40+6	86 (69)	80,431 (66)	**2.08 (1.48.2,93)**	37 (67)	**2.06 (1.22-3.47)**
≥41	23 (19)	29,009 (24)	1.06 (0.68.1,65)	10 (18)	1.07 (0.54-2.10)
Missing	*15*	*61,621*		*5*	
Induction:					
Total	60 (48)	36,885 (22)	**3.02 (2.16-4.22)**	30 (55)	**7.32 (4.41-12.15)**
Foley catheter	30 (24)	14,453 (8)	**3.22 (2.15-4.82)**	17 (31)	**4.62 (2.64-8.11)**
Prostaglandin	7 (6)	5,036 (3)	1.88 (0.88-4.02)	4 (7)	2.53 (0.92-6.98)
Oxytocin/ amniotomy	16 (13)	17,396 (11)	1.24 (0.74-2.09)	4 (7)	0.69 (0.25-1.91)
Missing	*7*	*22,024*		5	
Analgesia					
Analgesic - opiates	22 (18)	17,314 (9)	**1.80 (1.14.2,85)**	11 (20)	**2.40 (1.27-4.52)**
Epidural during labour	28 (22)	32,227 (18)	1.18 (0.78.1,79)	12 (22)	1.05 (0.55-2.03)
Epidural and analgesic – opiates	9 (7)	na		4 (7)	
Missing	*14*			*5*	

461 * Reference group from pregnant women in the Dutch Perinatal Registry (Perined) between March 1st
462 2017 – march 1st 2018
463 ** Odds Ratio between pregnant women with SARS-CoV-2 who have given birth and reference group
464 from Dutch Perinatal Registry
465 *** Odds Ratio between pregnant women with SARS-CoV-2 who were symptomatic at birth and
466 reference group from Dutch Perinatal Registry
467 na = not available
468
469

Table 4: Neonatal characteristics

	Neonates of women with SARS-CoV-2(%) N=137 n (%)	**Reference group of neonates * N=183,413 n (%)**	**OR (95% CI)** Pregnant women with SARS-CoV-2 compared with reference group
Level of Care			
No hospital admission	100 (79)	108,106 (70)	**2.32 (1.59-3.39)**
Neonatal ward	22 (17)	40,675 (26)	0.75 (0.48-1.19)
NICU (total)	4 (3)	6,030 (4)	0.97 (0.36-2.63)
Missing	*11*	46,189	
5' Apgar score			
≤ 4	2 (2)	2,944 (2)	0.91(0.22-3.67)
5-7	4 (3)	4,739 (3)	1.33 (0.62-3.06)
≥8	119 (95)	159,314 (95)	1.00 (0.61-1.64)
Missing	*12*	*16,416*	
Perinatal deaths (during labour or post-partum <28 days)	0	121	
Birthweight (median, IQR)			
Median	3360	3440	
IQR 25	2990	3080	
IQR 75	3795	3775	
missing	*17*	*16,521*	
Culture			
High vaginal tested positive	20 (20) 1 (5)	N/A	
Amniotic fluid tested positive	6 (6) 1 (17)	N/A	
Neonate tested positive	20 (17) 0	N/A	

* Reference group of neonates from pregnant women in the Dutch Perinatal Registry (Perined) between March 1st 2017 – march 1st 2018

** Odds Ratio between neonates of women with SARS-CoV-2 and reference group from the Dutch Perinatal Registry

Supporting information

Figure 1: Overview of reported positive cases by week