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

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Running title: Nationwide study of SARS-CoV-2 infection in pregnant women

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## Abstract

**Objective:** Describe characteristics, risk factors, maternal, obstetric and neonatal outcomes of SARS-CoV-2 infected pregnant women.

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

**Setting:** Nationwide study in the Netherlands.

**Population:** Pregnant women with confirmed SARS-CoV-2 infection admitted to hospital or in home-isolation: March 1<sup>st</sup>, 2020 - August 31<sup>st</sup>, 2020.

**Methods:** Pregnant women with positive PCR or antibody tests were registered using the Netherlands Obstetrics Surveillance System (NethOSS). (Selective) testing occurred according to national guidelines. Data from the national birth registry (pregnant pre-COVID cohort) and an age-matched cohort of COVID positive women (National Institute for Public Health and the Environment; fertile age COVID cohort) were used as reference.

**Main Outcome Measures:** Incidence of SARS-CoV-2 infection in pregnant women. Maternal, obstetric and neonatal outcomes including hospital and intensive care admission.

**Results:** Of 376 registered pregnant women with confirmed SARS-CoV-2 infection, 20% (74/376) were admitted to hospital, of whom 84% (62/74) due to SARS-CoV-2; 10% (6/62) were admitted to intensive care and 15% (9/62) to obstetric high care units. Risk factors for admission were non-European country of origin (OR 1.73, 95%CI 1.01-2.96) and being overweight/obese (OR 1.86, 95%CI 1.51-3.20). No maternal or perinatal deaths occurred. Caesarean section after labour-onset was increased (OR 1.58, 95%CI 1.09-2.28). Hospital and intensive care admission were higher compared to the fertile age COVID cohort (OR 6.75, 95%CI 5.18-8.81 and OR 2.52, 95%CI 1.11-5.77 respectively).

**Conclusions:** Non-European country of origin and being overweight/obese are risk factors for severe course of SARS-CoV-2 infection in pregnancy, risk of caesarean section and hospital and ICU admission are increased.

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*Keywords:* Pregnancy, COVID-19, SARS-CoV-2, Pregnancy complications, 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 SARS-CoV-2, has had a major impact worldwide.(1) High-risk populations have been identified, including the elderly, obese and ethnic minority groups. Evidence is increasingly showing 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)

It is known that pregnant women are not only more frequently affected by pneumonia, but their outcomes are often worse compared to non-pregnant women.(4, 5) Maternal physiological adaptations in pregnancy, and the physiological state of relative immune suppression, place pregnant women at increased risk of poor outcomes. It is likely that these mechanisms will also play a role in COVID-19. During previous coronavirus epidemics with SARS-CoV and MERS-CoV risk of maternal mortality and morbidity, as well as miscarriages and preterm labour were considerable. (6, 7)

A meta-analysis indicated that pregnant women may be at increased risk of ICU admission compared with age-matched non-pregnant women and that rates of vertical transmission appear to be very low. (8) A population-based cohort of pregnant women with SARS-CoV-2 admitted to UK hospitals showed an overrepresentation of women from black, Asian or other minority ethnic backgrounds and those with obesity or pre-existing medical conditions. (9) Since most studies have only reported on women admitted to hospital, it is unclear whether the risk of admission itself is increased among pregnant women, and whether findings in terms of risk groups can be generalised to all pregnant women with SARS-CoV-2. (8, 10)

In the present study, we have collected information on pregnant women with confirmed SARS-CoV-2 infection in the Netherlands, both in home-isolation and admitted to hospital. To provide health professionals with information on SARS-CoV-2 and pregnancy, crude numbers of collected cases were previously published on the website of the Dutch Society of Obstetrics and Gynaecology. (11) In-depth analysis or comparisons with reference groups are presented here.

The primary aim of this study was to investigate the incidence and maternal, obstetric and neonatal outcomes including hospital and ICU admission and medication use in pregnant women with SARS-CoV-2 infection. Secondary aims were a) to assess factors associated with a more severe course of disease and b) to explore the effect of pregnancy itself in women of fertile age with SARS-CoV-2 infection.



## Method

This is a multi-centre prospective nationwide population-based cohort study conducted between March 1<sup>st</sup>, 2020 and August 31<sup>st</sup>, 2020. 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.(12, 13) 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 NethOSS. All midwifery practices (N=577) were approached through the Society of Midwifery (KNOV), maternity care ('BO geboortezorg') and 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'), the Dutch Society of Paediatricians (NVK) and the Dutch National Institute for Public Health and the Environment (RIVM) indicated that all confirmed cases had to be reported to NethOSS.

In each of the 74 hospitals with an obstetrician-led maternity unit a NethOSS reporting physician or midwife was nominated to report cases on behalf of the perinatal cooperation group, based on the organization of Dutch birth care. Weekly requests were sent through email to reporting professionals. This email contained a reporting link specific to each reporter. Clinicians were asked to report any case meeting inclusion criteria or reply with '0' if they had no cases to report. For every reported case, information with regard to the woman's birth year, parity, estimated due date, date of positive SARS-CoV-2 test and information on hospital admission, management and birth was provided. Subsequently, a data collection form with additional questions was sent to each reporting physician or midwife. This 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.(14)

For nationwide comparison, two reference groups were established. One reference group consisted of pregnant women pre-COVID (pregnant pre-COVID cohort) using information from the Dutch Perinatal Registry (Perined). This registry contains population-based information pertaining to 99% of pregnancies in the Netherlands.(15) Specific information of all women in the registry who had given birth between March 1<sup>st</sup>, 2017 and March 1<sup>st</sup>, 2018, the most recent year with complete data, was used. A second reference group consisted of all women of fertile age (20-50 years) with SARS-CoV-2 (fertile age COVID cohort), regardless of pregnancy status, obtained through the National Institute for Public Health and the Environment (RIVM). These

women were confirmed SARS-CoV-2 positive by polymerase chain reaction (PCR) or imaging and registered until August 31<sup>st</sup>, 2020. It was unknown whether women were pregnant or not, so this group might also have included pregnant women. The number of ICU admissions was obtained from the National Intensive Care Evaluation (NICE), and the number of hospital admissions from the RIVM.

To study the main objective, that is to study characteristics of pregnant women with SARS-CoV-2 infection, we described the characteristics of the women enrolled in the NethOSS cohort and compared them to the pregnant pre-COVID cohort. To study the secondary aims, which are to assess factors associated with a more severe course of disease, we performed a nested case control within the NethOSS cohort (in hospital versus in home-isolation group) and comparison of the NethOSS cohort with the pregnant pre-COVID cohort. To explore the effect of pregnancy itself in women in fertile age with SARS-CoV-2 infection, we compared the NethOSS cohort with the fertile age COVID cohort.

Due to limited testing capacity, the testing policy from March 12<sup>th</sup>, 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. Pregnant women were at that time not considered a high-risk group.<sup>(16)</sup> Between March 12<sup>th</sup>, 2020 and April 30<sup>th</sup>, 2020, the policy of the RIVM stated that pregnant women required testing only in case of significant symptoms or if hospital admission due to SARS-CoV-2 related symptoms was required. Testing capacity was slowly increased and from April 30<sup>th</sup>, 2020 all people were asked to test if they had symptoms related to SARS-CoV-2 infection for longer than 24 hours. Because of this change in testing capacity, a sensitivity analysis was performed on the results before and after April 30<sup>th</sup>. The two available tests in the Netherlands were PCR using samples taken from the nose and throat, or a serological test based on presence of SARS-CoV-2 specific antibodies. Neonates born of SARS-CoV-2 positive mothers were tested for SARS-CoV-2 if signs or symptoms such as fever or increased infectious parameters were found.

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 including body mass index (BMI), age, country of origin, comorbidities and gestational age at onset of symptoms. For women who had given birth, mode of delivery, labour induction, analgesia, intrauterine or peripartum transmission and breastfeeding were assessed. Admission to hospital was defined by hospital stay for longer than 24 hours, but women admitted for birth

only were not included. Women at birth were divided into a symptomatic and an asymptomatic group. Women were considered symptomatic if complaints related to SARS-CoV-2 infection were reported at onset of labour. The incidence of SARS-CoV-2 infection was estimated using the most recently available data from Perined. In 2018, which included 79 962 pregnancies reported over a period of six months.

Country of origin was 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. Overweight pertained to BMI above 25 and obesity to a BMI above 30. Gestational age was based on first trimester dating ultrasound.

No core outcome sets were used in this study and the study did not have active patient involvement. No funding was received.

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 1<sup>st</sup>, 2020 and August 31<sup>st</sup>, 2020, 394 SARS-CoV-2 positive pregnant women were registered. In 18 pregnant women, a positive test result was reported, but additional information could not be retrieved. Additional data were returned for the remaining 376 women (95%). The estimated incidence of SARS-CoV-2 among pregnant women in the Netherlands over these six months was 4.70 per 1000 maternities. The number of collected cases was highest during the first two months of registration (March and April, N=216) with an estimated incidence of 8.10 per 1000 maternities. The number of positive cases per week can be seen in Figure S1. Testing capacity increased after April 30<sup>th</sup>. In March and April 57/216 (26%) women were admitted, May to September 17/160 (11%) women were admitted. Sensitivity analysis between cases before and after April 30<sup>th</sup> did not affect our general conclusions.

The majority of pregnant women with SARS-CoV-2 were not admitted to hospital (302/376, 80%). Instead, they stayed, as advised by the government, in home-isolation until symptoms had subsided and two weeks after disease-onset. Of pregnant women with SARS-CoV-2 admitted to hospital (74/376, 20%), admission was COVID-related in 62/74 (85%). Other reasons for admission were signs of imminent premature birth and hypertensive disorders. Six women required ICU treatment, which represents 10% (6/62) of all pregnant women with SARS-CoV-2 admitted to hospital and 2% (6/376) of all registered pregnant women with SARS-CoV-2. Another nine (9/62, 15%) were admitted to high obstetric care units with additional monitoring facilities but did not require mechanical ventilation. No maternal death was reported.

Signs of pneumonia on imaging were found in 35/376 (9%) registered pregnant women. They most frequently complained of cough (180/376, 47%), breathlessness (91/376, 24%), flu-like symptoms (95/376, 25%) and fever (149/376, 39%). Antibiotics were administered in 41/376 (11%) women and antiviral drugs in 5/376 (1%) (oseltamivir, N=2, remdesivir, N=3). In 14/376 (4%), corticosteroids were administered to stimulate fetal lung maturation. This was due to signs of threatening preterm labour (7/14, 50%) or high risk of iatrogenic preterm labour due to the severity of SARS-CoV-2 infection (7/14, 50%). Oxygen supplementation was used in 30/376 women (8%) with signs of breathlessness and low oxygen levels. Four pregnant women (4/376, 1%) needed mechanical ventilation of whom three were ventilated in prone position.

An overview of background characteristics of pregnant women with SARS-CoV-2 and comparison with the pregnant pre-COVID cohort is shown in Table 1. In Table 2 pregnant women with SARS-CoV-2 requiring hospital admission were compared with pregnant women with SARS-

CoV-2 in home-isolation. Among pregnant women testing positive for SARS-CoV-2, non-European women were disproportionately present in comparison to the pregnant pre-COVID cohort (OR 8.96, 95%CI 6.71-10.42) and among pregnant women with SARS-CoV-2 admitted to hospital compared to those in home-isolation (OR 1.73, 95%CI 1.01-2.96). Overweight or obese pregnant women with SARS-CoV-2 were also more often admitted to hospital compared to women in home-isolation (OR 1.86, 95%CI 1.08-3.20). Pregnant women with SARS-CoV-2 more often experienced signs of imminent premature labour compared with the pregnant pre-COVID cohort (OR 2.37, 95%CI 1.47-3.82). Risk of hospital admission was decreased in the first trimester (OR 0.01, 95%CI 0.00-0.03).

Six women had a miscarriage and intrauterine fetal death occurred in one pregnant woman with SARS-CoV-2. This was a term pregnancy, and the cause of intrauterine death was unknown. Swabs of amniotic fluid, fetus and placenta were negative for SARS-CoV-2.

Information concerning birth was retrieved for 289 pregnant women with SARS-CoV-2 (289/376, 77%) and summarized in Table 3. Results of pregnant women with SARS-CoV-2 and a subgroup of those symptomatic at birth (N=70) were compared with the pregnant pre-COVID cohort. The risk of caesarean section after onset of labour was increased (OR 1.58, 95%CI 1.09-2.28), especially for women symptomatic at birth (OR 2.29, 95%CI 1.20-4.36). Pre-labour caesarean section was performed in 20 women (20/289, 7%). In only one woman the indication was COVID-related. Reasons for caesarean section after labour-onset (32/289, 11%) of pregnant women with SARS-CoV-2 were obstructed labour (13/32, 41%) suspected fetal distress (13/32, 41%), both obstructed labour and suspected fetal distress (2/32, 6%) or other (4/32, 13%). Compared with the pregnant pre-COVID cohort, labour was more often induced in pregnant women with SARS-CoV-2 (OR 4.05, 95%CI 3.18-5.17). The risk of preterm birth (OR 1.01, 95%CI 0.68-1.49) was not increased for all pregnant women with SARS-CoV-2 infection; however, it was increased for women symptomatic at birth (OR 2.02, CI95% 1.11-3.69).

An overview of neonatal results can be found in Table 4. No cases of vertical transmission or neonatal death were reported. There were six multiple pregnancies and one intra-uterine fetal death, resulting in 295 live births. Of these, 47/295 (17%) neonates were admitted to a neonatal unit. Three neonates were admitted due to suspicion of infection. Out of 24 neonates tested; no neonate tested positive for SARS-CoV-2.

Hospital and ICU admission of pregnant women with SARS-CoV-2 were also compared to the fertile age COVID cohort (of whom some were pregnant). Of 19,110 women testing positive for SARS-CoV-2 669/19,110 (3.5%) were admitted to hospital and 122/19,110 (6%) to ICU. ORs for hospital and ICU admission were considerably increased: OR 6.75, 95%CI 5.18-8.81 and OR 2.52, 95%CI 1.11-5.77 respectively.

## **Discussion**

### *Main findings*

This large nationwide population-based registration study (NethOSS) provides outcomes of pregnant and postpartum women in the Netherlands who had been infected with SARS-CoV-2, during the first wave up to August 31<sup>st</sup>, 2020. No maternal mortality was reported. Among pregnant women with SARS-CoV-2 admitted to hospital compared to home-isolation, those who were overweight and from non-European countries of origin were overrepresented. Labour induction was more common among pregnant women with SARS-CoV-2 and pregnant women with SARS-CoV-2 had a higher risk of caesarean section after labour-onset especially when symptomatic at birth compared with a pregnant pre-COVID cohort. Risk of preterm birth was only elevated for pregnant women symptomatic at birth. No vertical transmission was reported. Pregnant women with SARS-CoV-2 were at higher risk of hospital admission, especially obstetric high care and ICU compared to a cohort of women with SARS-CoV-2 in the same age group (fertile COVID cohort).

### *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. 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 high case ascertainment. RIVM stopped reporting the number of pregnant women positive for SARS-CoV-2 after April 2<sup>nd</sup>, 2020. They had reported 78 cases by that date, compared with 98 cases reported to NethOSS.(17) 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, tests were initially limited to people with significant symptoms requiring hospital admission (from March 12<sup>th</sup> to April 30<sup>th</sup>, 2020). Therefore, some underreporting of SARS-CoV-2 infections is possible. Moreover, since women with mild symptoms were not always tested and consequently not included in this study, associations with infection may appear worse than they are. Testing was expanded from May 1<sup>st</sup>, which is likely to have resulted in more women with mild or no symptoms being included in our study. However, since the number of SARS-CoV-2 infections in the Netherlands was generally

much lower between May 1<sup>st</sup> and August 31<sup>st</sup>, women with mild or no symptoms may still be underrepresented.

We compared outcomes of pregnant women with SARS-CoV-2 to a reference group of pregnant women without SARS-CoV-2 infection between 2017-2018 (pregnant pre-COVID cohort), which was the most recent available year with complete data. Recent studies, however, also imply a general effect of the lockdown for example on premature birth rates and birth weight. (18, 19) We have not been able to assess these general effects in our study.

Registration is still ongoing, and some women analysed in this report were still pregnant at the time of writing (N=81). The effect of SARS-CoV-2 on pregnancy, birth and newborns could therefore not be assessed for this group. With a second wave of SARS-CoV-2 infection ongoing, it is crucial to analyse perinatal outcomes including that of women infected in the first and second trimester, since these data have only been scarcely reported.(8)

### *Interpretation*

Even though the majority of pregnant women with SARS-CoV-2 infection experienced mild symptoms, a small but significant group developed severe morbidity. This study recognizes several risk factors for hospital admission of pregnant women such as increased BMI and non-European background. When comparing results of pregnant women to those of all fertile women in the same age group, the pregnant women in our study were more often admitted to hospital and ICU. The reference group contained women until 50 years of age. Since risk of hospital admission is reported to increase with age, and pregnant women in our study population above 40 years of age were scarce (8%) and above 45 years absent, we assume that the risk could be even higher when compared with women up to 40 years of age.(20) This reference group will also have included some pregnant women, since pregnancy was not registered by RIVM or NICE. This may have reduced the OR, since pregnant women with higher risk of admission were also included in the reference group. This is the first study to show 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. (8, 21)

The incidence of SARS-CoV-2 infection among pregnant women in the Netherlands was 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.(22)



Most other reported studies are facility-based.(9, 23) 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). This highlights the importance of a registration system such as NethOSS which enables rapid data collection, for instance in case of a pandemic.

An increased risk of caesarean section after labour-onset was demonstrated in SARS-CoV-2 infected women, especially when they had symptoms at birth. Similar increases have been reported in the United Kingdom, Italy and New York City.(9, 23, 24) This might be due to increased caution of the attending physician or 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. Neonatal outcomes in our study were reassuring and similar to results in other studies.(8)

To guide therapy and vaccination policies in the vulnerable group of pregnant women, especially subgroups at risk of severe disease, international IPD meta-analysis based on robust population-based data is warranted within INOSS, where in 17 countries uniform data on hospital admitted SARS-CoV-2 positive pregnant women were collected. Long-term consequences of SARS-CoV-2 infection for women and their babies remain unknown and are also urgently needed. (25-29)

## Conclusions

It is increasingly clear that pregnant women may comprise a vulnerable group in the COVID-19 pandemic. In the Netherlands, not being of European countries of origin and being overweight or obese were risk factors for hospital admission. Infected women had higher odds of being induced or giving birth by caesarean section. Pregnant and postpartum women infected with SARS-CoV-2 appear to be at higher risk of hospital and ICU admission compared to COVID positive women in the same age group. 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, TvdA 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=376 n (%)	Reference group of pregnant women (pregnant pre-COVID cohort)* N=183,413 n (%)	OR (95% CI) <sup>1</sup>  Pregnant women with SARS-CoV-2 versus reference group
<b>General</b>			
Age			
<25	26 (7)	16,662 (9)	0.75 (0.50-1.11)
25-30	97 (26)	54,837 (30)	0.82 (0.65-1.03)
30-35	153 (41)	70,615 (39)	1.10 (0.90-1.35)
35-40	71 (19)	34,290 (19)	1.01 (0.78-1.32)
>40	28 (7)	6,913 (4)	<b>2.06 (1.40-3.03)</b>
Missing	1	96	
Country of origin			
European	189 (58)	161,464 (90)	<b>0.16 (0.13-0.20)</b>
African	69 (21)	5 (0)	
Asian	19 (6)	7,401 (4)	1.44 (0.91-2.29)
South American	5 (2)	4,681 (3)	0.58 (0.24-1.41)
Other	45 (14)	6,599 (4)	<b>4.17 (3.05-5.72)</b>
Missing	49	3,263	
BMI			
Normal (<25)	161 (49)	na	
Overweight (25-30)	100 (30)	na	
Obese (>30)	67 (20)	na	
Missing	48		
Smoking			
Current	16 (5)	na	
Missing	43	na	
Pre-existing medical problems			
Pulmonary disease	23 (7)	na	
Cardiac disease	6 (2)	na	
Diabetes	6 (2)	na	
Missing	34		

<b>Pregnancy</b>			
Parity			
Nulliparous	159 (42)	79,518 (43)	0.95 (0.78-1.17)
Multiparous	217 (58)	103,549 (56)	1.05 (0.85-1.29)
Missing	0	346	
Trimester at positive test			
1 <sup>st</sup> trimester	49 (13)	N/A	
2 <sup>nd</sup> trimester	101 (27)	N/A	
3 <sup>rd</sup> trimester	200 (54)	N/A	
Postpartum	19 (5)	N/A	
Missing	7		
Multiple pregnancy	9 (2)	5,270 (3)	0.91 (0.47-1.77)
Missing	33	41	
Signs of premature labour	18 (5)	4,226 (2)	<b>2.37 (1.47-3.82)</b>
Missing	40	2197	

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

<sup>1</sup> 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: pregnant women admitted to hospital compared with pregnant women in home-isolation**

Characteristics	Pregnant women admitted to hospital N=74 n (%)	Pregnant women in home-isolation N=302 n (%)	OR (95% CI)*  Hospital admission versus home-isolation
<b>General</b>			
<b>Age</b>			
<25	4 (5)	22 (7)	0.73 (0.24-2.17)
25-30	15 (20)	82 (27)	0.68 (0.37-1.26)
30-35	36 (49)	117 (39)	1.49 (0.89-2.49)
35-40	13 (18)	58 (19)	0.89 (0.46-1.73)
>40	6 (8)	22 (7)	1.12 (0.44-2.87)
Missing	0	1	
Country of origin			
European	32 (47)	157 (61)	<b>0.58 (0.34-0.99)</b>
African	17 (25)	52 (20)	1.33 (0.71-2.49)



Asian	5 (7)	14 (3)	<b>1.39 (0.48 -4.00)</b>
South American	2 (3)	3 (1)	2.59 (0.42-15.79)
Other	12 (18)	33 (13)	1.47 (0.71-3.02)
<i>Missing</i>	6	43	
BMI			
Normal (<25)	26 (37)	135 (52)	<b>0.54 (0.31-0.93)</b>
Overweight (25-30)	25 (36)	75 (29)	1.36 (0.78-2.37)
Obese (>30)	19 (27)	48 (19)	1.63 (0.88-3.01)
Missing	4	44	
Smoking			
Current	8 (11)	8 (3)	<b>4.03 (1.46-11.16)</b>
<i>Missing</i>	3	40	
Pre-existing medical problems			
Pulmonary disease	6 (8)	17 (6)	1.35 (0.51-3.57)
Cardiac disease	2 (3)	4 (1)	1.90 (0.34-10.59)
Diabetes	1 (1)	5 (2)	0.75 (0.09-6.49)
<i>Missing</i>	2	32	
<b>Pregnancy</b>			
Parity			
Nulliparous	32 (43)	127 (42)	1.05 (0.63-1.76)
Multiparous	42 (57)	175 (58)	0.95 (0.57-1.59)
Missing	0	0	
Trimester at positive test			
1 <sup>st</sup> trimester	4 (5)	156 (53)	<b>0.01 (0.00-0.03)</b>
2 <sup>nd</sup> trimester	14 (19)	7 (2)	0.56 (0.30-1.05)
3 <sup>rd</sup> trimester	44 (60)	7	1.31 (0.78-2.19)
Postpartum	12 (16)	7 (3)	<b>7.96 (3.01-21.04)</b>
<i>Missing</i>	0	32	
Multiple pregnancy	2 (3)	6 (2)	1.06 (0.22-5.21)
<i>Missing</i>	1	39	
Signs of premature labour	12 (16)		<b>8.43 (3.04-23.34)</b>
<i>Missing</i>	1		

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

**Table 3: Birth characteristics**

	<b>Pregnant women with SARS-CoV-2 who have given birth</b>	<b>Pregnant pre-COVID cohort, pregnant women who have given birth*</b>	<b>OR (95% CI)**</b> Pregnant women with SARS-CoV-2 compared with pregnant pre-COVID cohort	<b>Pregnant women with SARS-CoV-2 who were symptomatic at birth</b>	<b>OR (95% CI)***</b> Pregnant women with SARS-CoV-2 who were symptomatic compared with pregnant pre-COVID cohort
	<b>N=289</b> <b>n (%)</b>	<b>N=183,413</b> <b>n (%)</b>		<b>N=70</b> <b>n (%)</b>	
<b>Mode of birth:</b>					
Vaginal birth	227 (79)	123,709 (76)	1.31 (0.92-1.76)	43 (61)	<b>0.50 (0.31-0.80)</b>
Instrumental vaginal birth	17 (6)	12,802 (8)	0.75 (0.46-1.22)	6 (9)	1.09 (0.47-2.53)
Pre-labour caesarean section	20 (7)	13,477 (8)	0.85 (0.54-1.33)	10 (14)	1.84 (0.94-3.59)
Caesarean section after onset of labour	32 (11)	12,203 (8)	<b>1.58 (1.09-2.28)</b>	11 (16)	<b>2.29 (1.20-4.36)</b>
Missing	8	21,222		0	
<b>Gestational age at birth</b>					
16+0 - <36+6	28 (10)	12,352 (10)	1.01 (0.68-1.49)	13 (19)	<b>2.02 (1.11-3.69)</b>
37-40+6	196 (72)	80,431 (66)	1.29 (0.99-1.68)	47 (67)	<b>1.05 (0.64-1.73)</b>
>41	50 (18)	29,009 (24)	0.71 (0.53-0.97)	10 (14)	0.53 (0.27-1.04)
Missing	15	61,639		0	
<b>Induction:</b>					
Total	107 (39)	36,885 (22)	<b>4.05 (3.18-5.17)</b>	32 (46)	<b>5.47 (3.41-8.78)</b>
Foley catheter	65 (61)	14,453 (8)	<b>3.16 (2.39-4.18)</b>	18 (58)	<b>3.59 (2.10-6.14)</b>
Prostaglandin	11 (10)	5,036 (3)	1.30 (0.71-2.38)	6 (19)	<b>2.96 (1.28-6.84)</b>
Oxytocin/amniotomy	31 (29)	17,396 (11)	1.07 (0.74-1.56)	4 (13)	0.52 (0.19-1.42)
Missing	15	22,024		1	
<b>Analgesia</b>					
Analgesic - opiates	36 (13)	17,314 (9)	0.82 (0.58-1.17)	15 (22)	1.65 (0.93-2.93)
Epidural during labour	72 (25)	32,227 (18)	0.88 (0.67-1.15)	17 (25)	0.89 (0.51-1.54)

Epidural and analgesic – opiates	11 (4)	na		2 (3)	
<i>Missing</i>	3	67,115		3	

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

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

\*\*\* Odds Ratio between pregnant women with SARS-CoV-2 who were symptomatic at birth and reference group from Dutch Perinatal Registry

na = not available

**Table 4: Neonatal characteristics**

	<b>Neonates of women with SARS-CoV-2(%)</b>	<b>Pregnant pre-COVID cohort neonates*</b>	<b>OR (95% CI)**</b>
	<b>N=295</b>	<b>N=201,000</b>	Pregnant women with SARS-CoV-2 compared with pregnant pre-COVID cohort neonates
	<b>n (%)</b>	<b>n (%)</b>	
<b>Level of Care</b>			
No hospital admission	231 (83)	108,106 (70)	<b>2.12 (1.55-2.91)</b>
Neonatal ward	47 (17)	40,675 (26)	<b>0.57 (0.42-0.78)</b>
NICU (total)	7 (3)	6,030 (4)	0.64 (0.30-1.35)
<i>Missing</i>	17	46,189	
<b>5' Apgar score</b>			
< 4	2 (1)	2,944 (2)	0.55 (0.14-2.21)
5-7	8 (3)	4,739 (3)	1.04 (0.51-2.10)
>8	262 (96)	159,314 (95)	1.26 (0.67-2.38)
<i>Missing</i>	23	34,003	
Perinatal deaths (during labour or post-partum <28 days)	0	121 (0.06)	

Birthweight (median, IQR)***			
Median	3519	3440	
IQR 25	3008	3080	
IQR 75	3762	3775	
<i>missing</i>	<i>17</i>	<i>16,521</i>	
Culture			
High vaginal tested positive	21 (9) 1 (5)	N/A	
Amniotic fluid tested positive	7 (3) 1 (14)	N/A	
Neonate tested positive	24 (10) 0	N/A	
<i>Missing</i>	<i>50</i>		

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

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

\*\*\* birthweight in grams

N/A = not applicable