

# COVID-19 in pregnancy—characteristics and outcomes of pregnant women admitted to hospital because of SARS-CoV-2 infection in the Nordic countries

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## Abstract

**Introduction:** Population-based studies about the consequences of SARS-CoV-2 infection (COVID-19) in pregnancy are few and have limited generalizability to the Nordic population and healthcare systems.

**Material and methods:** This study examines pregnant women with COVID-19 in the five Nordic countries. Pregnant women were included if they were admitted to hospital between 1 March and 30 June 2020 and had a positive SARS-CoV-2 PCR test  $\leq 14$  days prior to admission. Cause of admission was classified as obstetric or COVID-19-related.

**Abbreviations:** BMI, body mass index; CD, cesarean delivery; COVID-19, SARS-CoV-2 disease with symptoms; ICU, intensive care unit; Iceland, Iceland; INOSS, International Network of Obstetric Survey Systems; MBRN, Medical Birth Registry of Norway; NICU, Neonatal Intensive Care Unit; NIPH, Norwegian Institute of Public Health; NOSS, Nordic Obstetric Surveillance Study.

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**Results:** In the study areas, 214 pregnant women with a positive test were admitted to hospital, of which 56 women required hospital care due to COVID-19. The risk of admission due to COVID-19 was 0.4/1000 deliveries in Denmark, Finland and Norway, and 3.8/1000 deliveries in the Swedish regions. Women hospitalized because of COVID-19 were more frequently obese ( $p < 0.001$ ) and had a migrant background ( $p < 0.001$ ) compared with the total population of women who delivered in 2018. Twelve women (21.4%) needed intensive care. Among the 56 women admitted due to COVID-19, 48 women delivered 51 infants. Preterm delivery ( $n = 12$ , 25%,  $p < 0.001$ ) and cesarean delivery ( $n = 21$ , 43.8%,  $p < 0.001$ ) were more frequent in women with COVID-19 compared with women who delivered in 2018. No maternal deaths, stillbirths or neonatal deaths were reported.

**Conclusions:** The risk of admission due to COVID-19 disease in pregnancy was low in the Nordic countries. A fifth of the women required intensive care and we observed higher rates of preterm and cesarean deliveries. National public health policies appear to have had an impact on the risk of admission due to severe COVID-19 disease in pregnancy. Nordic collaboration is important in collecting robust data and assessing rare outcomes.

#### KEY WORDS

cohort studies, COVID-19, obstetric delivery, pregnancy, pregnancy complications, pregnancy outcome, prospective studies, severe acute respiratory syndrome coronavirus 2

#### Key message

Risk of hospital admission due to COVID-19 infection among pregnant women was low in the Nordic countries, but varied between the countries, most likely related to different national public health strategies.

## 1 | INTRODUCTION

The World Health Organization declared a global pandemic of coronavirus disease in March 2020.<sup>1</sup> During the H1N1 influenza pandemic, pregnant women were particularly vulnerable, resulting in increases of maternal and perinatal mortality among those infected.<sup>2-8</sup> Systematic review and meta-analysis by WHO about the effect of COVID-19 in pregnancy identified preexisting comorbidities and high maternal age and body mass index (BMI) as risk factors for severe infection.<sup>9</sup> Preterm birth rate increased among infected women.<sup>9</sup> Recent publications from the USA indicate that pregnant women are at higher risk for serious COVID-19 disease compared with non-pregnant women.<sup>10,11</sup> These studies and the majority of studies in the WHO systematic review were performed in settings with limited generalizability to the Nordic populations and healthcare systems. With the on-going pandemic, population-based studies with larger case numbers and lower risk of bias are crucial for guiding disease surveillance and health management.<sup>12</sup> A few population-based studies assessing the risk and consequences of COVID-19 infection in pregnancy have been published.<sup>13-15</sup> However, the inclusion criteria comprised all causes of hospital admission, resulting in heterogeneous study populations.

The population in the Nordic countries is relatively uniform, and healthcare during pregnancy is provided free of charge. All five countries have medical birth registries with mandatory registrations of maternal and fetal/neonatal outcomes of all births.

The objective of this study was to describe hospital admissions of pregnant women with COVID-19 in the Nordic countries. We present preliminary, aggregated results including the characteristics and medical risk factors, clinical management and outcomes of pregnant women with COVID-19, focusing primarily on the group of women admitted due to COVID-19, during the first 4 months of the pandemic in the Nordic countries.

## 2 | MATERIAL AND METHODS

This study is an ongoing prospective observational study in the Nordic countries and part of the Nordic Obstetric Surveillance Study (NOSS) collaboration. The study includes pregnant women with COVID-19 infection and hospital admission for at least 24 hours. COVID-19 infection was defined as detection of viral RNA on a pharyngeal swab  $\leq 14$  days prior to hospital admission. Cause of admission was classified as obstetric, for example, delivery or obstetric complaints, or COVID-19-related.

Primary outcomes included maternal or neonatal admission to intensive care unit (ICU or NICU), COVID-19 pneumonia, maternal mortality (deaths during pregnancy or within 42 days after the end of pregnancy), preterm delivery (delivery before 37 completed weeks of gestation) and perinatal mortality (stillbirth from 22 completed weeks of gestation and first week neonatal deaths). We collected information on sociodemographic risk factors (partner status, migrant background, occupation), pregestational chronic diseases (including cardiac, renal, endocrine, psychiatric, hematologic and autoimmune disease, cancer and HIV), gestational age at COVID-19 infection, and clinical care such as induction of labor and mode of delivery.

Calculation of BMI was based on pregestational weight or first recorded weight in pregnancy. Gestational age was based on estimated date of delivery assessed by ultrasound according to national guidelines, or according to last menstrual period for women without an ultrasound dated pregnancy at the time of COVID-19 infection.

Data were entered into a uniform case report form, adapted in each country.

In Denmark, all obstetric units participated. A clinician in each unit prospectively reported cases to a joint electronic database in EASYTRIAL (easytrial.net, Denmark). Reminders were sent out to secure data completeness and cases were validated by a retrospective registry linkage, with data obtained from the Danish National Patient Register, the Danish National Service Register and the Danish Microbiology Database every second month. Missing cases identified by validation were entered retrospectively.

In Finland, cases admitted to Helsinki University Hospital were included. Most of the COVID-19 patients in Finland during the study period were inhabitants of the Helsinki region (73%,  $n = 19$ ), and fewer than three cases were reported to have been admitted to the other university hospitals by November 2020 (O Åyräs pers. corres.). Consequently, data collection from Helsinki University Hospital alone is assumed to have included most affected cases. Data were entered into the report form by one primary investigator.

In Iceland, public health authorities recorded all cases of COVID-19, and information about all pregnant women with COVID-19 was forwarded to the Icelandic Birth Registry. Cases were validated by a retrospective registry linkage with data obtained from the Icelandic National Patient Register and the Icelandic Birth Register. Data were entered into the report form by one primary investigator.

In Norway, data were prospectively collected by the Medical Birth Registry of Norway (MBRN) at the Norwegian Institute of Public Health (NIPH). All hospitals providing care for pregnant women participated. Reminders were sent out bimonthly. Data were entered using an online form to a safe research server at Service for Sensitive Data (TSD), University of Oslo, contracted by MBRN/NIPH.

In Sweden, data were included from three institutions: Karolinska University Hospital (KUH), Sahlgrenska University Hospital (SaUH) and Skåne University Hospital (SkUH). These institutions are among the major referral hospitals in the country and account for 22% of annual deliveries in Sweden. Data were retrieved from Hospital Discharge Registers and medical records at each

participating obstetric unit and entered into a joint electronic database in REDCap<sup>16,17</sup> hosted at Lund University.

The study sample size was governed by the disease incidence, so no formal power calculation was performed.

Results are reported both for all five countries and but are restricted to Denmark, Finland, Iceland and Norway to account for potential selection bias in the Swedish data, where only tertiary centers were included. Nominal data are presented as numbers and percentages. Continuous variables are presented as the range of country means when normally distributed and when not normally distributed as range of country medians. Comparison data for all deliveries in 2018, the most recent year for which complete data were available, were collected from the national Medical Birth Registry websites,<sup>18-21</sup> and using unpublished statistics provided by the registries. The total number of deliveries was based on the number of deliveries during the study period in Norway and at the included Swedish sites, and an estimation based on the number of annual deliveries in 2019 in Denmark, Finland and Iceland. Chi-square tests were used to assess differences in outcome frequencies between the cases and the comparison population.

Data analyses were performed using IBM SPSS Statistics 21 (IBM Corp., Armonk, NY, USA) and STATA 16SE (STATA CORP LLC, College Station, TX, USA).

## 2.1 | Ethical approval

National ethical approval was obtained from the following authorities:

Denmark: Danish Patient Safety Authority (reg. no. 31-1521-252: 24 April 2020) and the regional Data Protection Agency in Region Zealand (reg. no. REG-022-2020: 23 March 2020)

Finland: Helsinki University Hospital. (reg. no. HUS1624/2020: 13 May 2020)

Iceland: Landspítali University Hospital, the National Bioethics Committee (reg. no. VSNb2020050016/03.0I: 25 June 2020) and the Icelandic Data Protection Authority (reg. no. 20-106: 9 June 2020)

Norway: Norwegian Institute of Public Health, Data, Protection Officer (reg. no. 20\_11054: 3 April 2020) and the Western Regional Ethics Committee (reg. no. 125890: 26 March 2020)

Sweden: the Swedish Ethical Review Authority (reg. no. 2020-03012: 11 August 2020 for SUH and SKH and reg. no. 2020-01499: 22 April 2020 for KUH).

In Denmark, Iceland, Norway and KUH, ethical approval excluded the studies on the principle of individual consent. In Finland, ethical approval is not required in register-based studies. In SaUH and SkUH, women received written information about the study, including an opt-out possibility. Data were managed and stored in accordance with national regulations and the General Data Protection Regulation (GDPR). National numbers <3 are not presented to avoid identification.

### 3 | RESULTS

Between 1 March and 30 June 2020, we identified 214 pregnant women who were admitted to hospital for any reason with a positive SARS-CoV-2 PCR test  $\leq 14$  days prior to hospital admission. No women opted out in Sweden. The risk of hospital admission was 0.8/1000 deliveries, ranging from 0.5 to 1.0/1000 in Denmark, Finland, Iceland and Norway, and 18.2/1000 in the Swedish regions.

Due to different national and regional testing strategies (Table S1) the study groups in the various countries were heterogeneous, with more women with asymptomatic/mild COVID-19 admitted for delivery or obstetric care in countries/regions with universal screening. Characteristics of women admitted for any reason are shown in Table S2. We therefore restricted further analyses to the pregnant

women who required hospital admission because of COVID-19 disease, as shown in the flowchart (Figure 1).

Fifty-six pregnant women required hospital care for COVID-19 disease. There were no admissions in Iceland and the risk of hospital admission was 0.4/1000 deliveries (range 0.3–0.5) in Denmark, Finland and Norway, and 3.8/1000 in the Swedish regions.

Figure 2 illustrates the gestational age at first positive SARS-CoV-2 test among the included women. Most women admitted due to COVID-19 were in the third trimester of pregnancy when they tested positive. Figure S2 shows the month of first positive test and thus illustrates the pandemic timeline.

Characteristics of the pregnant women admitted due to COVID-19 are presented together with the Medical Birth Registry data from 2018 in Table 1. Compared with the women who delivered in 2018, women admitted due to COVID-19 were more frequently obese, had BMI  $>30$  ( $p < 0.001$ ) and were migrants ( $p < 0.001$ ).

In the Swedish regions, relatively more women admitted due to COVID-19 had preexisting chronic diseases compared with the other Nordic countries (Sweden:  $n = 14/36$ ; 38.9%, Denmark, Finland, Iceland, Norway:  $n = 2/20$ ; 10%). The Swedish women had positive SARS-CoV-2 tests later in pregnancy and therefore also had a shorter interval between test and delivery.

The maternal and fetal/neonatal outcomes and clinical care are presented in Table 2. Among the 56 cases, 12 women were admitted to ICU (21.4%). No maternal deaths were reported. During the study period, 48 women delivered 51 infants. Compared with 2018 deliveries, more women admitted due to COVID-19 had a cesarean delivery (CD) (41.7 vs 17.3%,  $p < 0.001$ ), and the proportion of emergency CD was higher (85.0 vs 53.8%,  $p = 0.003$ ). The risk of preterm delivery was also increased (25% vs 5.7%,  $p < 0.001$ ). Seven neonates were admitted to NICU (13.7%) and no stillbirths or neonatal deaths were reported.

In the Swedish regions, induction of labor among the COVID-19 infected women was more frequent than in the other Nordic countries (Sweden:  $n = 11/31$ , 35.5%; Denmark, Finland, Iceland, Norway:  $n = 5/17$ , 29.4%) but fewer women had a CD (Sweden:  $n = 12/31$ , 38.7%; Denmark, Finland, Iceland, Norway:  $n = 9/17$ ; 52.9%).

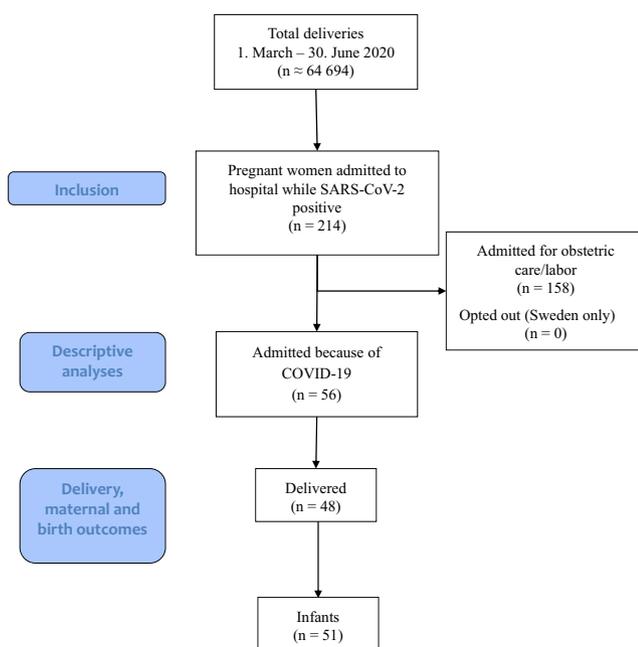


FIGURE 1 Flow diagram [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

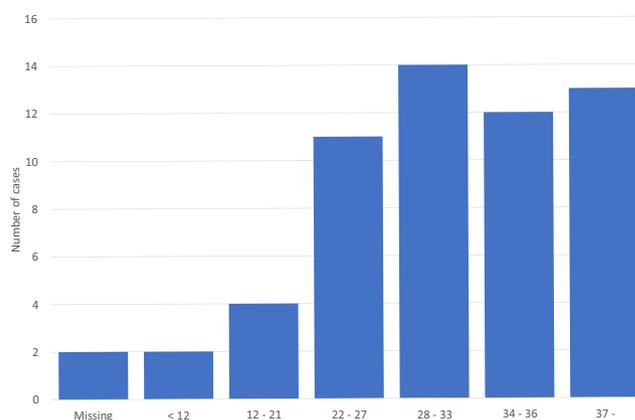


FIGURE 2 Completed gestational week at first positive SARS-CoV-2 PCR test in 56 pregnant women admitted to hospital due to COVID-19 in the Nordic countries between 1 March and 30 June 2020 [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



**TABLE 2** Clinical care, delivery, maternal and neonatal outcomes of pregnant women admitted to hospital because of COVID-19 infection in the Nordic countries between 1 March and 30 June 2020, compared with the characteristics of women who delivered in 2018

	NOSS COVID-19 admissions		NOSS COVID-19 admissions vs deliveries in 2018		NOSS COVID-19 admissions vs deliveries in 2018	
	NOSS COVID-19 admissions	Deliveries in the Nordic countries, 2018 <sup>a</sup>	NOSS COVID-19 admissions vs deliveries in 2018 p-value <sup>b</sup>	Deliveries in Denmark, Finland, Iceland, Norway 2018 <sup>a</sup>	NOSS COVID-19 admissions vs deliveries in 2018 p-value <sup>b</sup>	Deliveries in Denmark, Finland, Iceland, Norway 2018 <sup>a</sup>
Total deliveries <sup>c</sup>	~64 694	286 868		~55 255		167 779
Cases	56			20		
GA at first positive SARS-CoV-2 test, range of country medians	25+5 to 35+2 weeks			25+2 to 28+0 weeks		
Interval between first positive SARS-CoV-2 test and delivery, days, range of country medians	31–97			68–97		
Pneumonia confirmed by imaging, n (%)	32 (57.1)			8 (40)		
Admission to ICU, n (%)	12 (21.4)			4 (20)		
Maternal death, n (/100,000)	0 (0)	6.8 to 8.1 <sup>d</sup>		0		
Delivery outcomes						
Delivered, n (%)	48 (85.7)			17 (85.0)		
Induction of labor, n (%)	16 (33.3)	61592 (21.8)	0.05	5 (29.4)		43 307 (25.8)
Mode of delivery						
Vaginal delivery, n (%)	28 (58.3)	233 929 (82.7)	<0.001	8 (47.1)		138 800 (82.7)
Cesarean delivery (CD)	20 (41.7)	49 031 (17.3)	<0.001	9 (52.9)		28 979 (17.3)
Emergency CD, n (% of all CD)	17 (85.0)	26 367 (53.8)	0.003	>6		17 542 (60.5)
Elective CD, n (% of all CD)	3 (15.0)	22 529 (45.9)	0.003	<3		11 383 (39.3)
Preterm delivery GA <37w, n (%)	12 (25.0)	16 211 (5.7)	<0.001	5 (29.4)		9 936 (5.9)
Infant outcomes						
Live birth, n (%)	51 (100)	286 939 (99.7)	0.686	18		169 724 (99.7)
GA at delivery, range of country medians	35+4 to 40+1 weeks			35+4 to 40+1 weeks		
NICU admission, n (%)	7 (13.7)			<3 (<10)		5 (27.8)
Stillbirth <sup>e</sup> n (/1000)	0	975 (0.34)	na	0		539 (0.32)

Continues

TABLE 2 (Continued)

	NOSS COVID-19 admissions		Deliveries in the Nordic countries, 2018 <sup>a</sup>		NOSS COVID-19 admissions vs deliveries in 2018 p-value <sup>b</sup>		NOSS COVID-19 admissions vs deliveries in 2018 Denmark, Finland, Iceland, Norway p-value <sup>b</sup>	
	NOSS COVID-19 admissions	0	Deliveries in the Nordic countries, 2018 <sup>a</sup>	520 (1.8)	Deliveries in Denmark, Finland, Iceland, Norway 2018 <sup>a</sup>	368 (2.2)	na	na
Neonatal death <sup>f</sup> , n (/1000)	0	0	0	0	0	0	0	na

Note: All websites were accessed 25 or 26 November 2020.

Abbreviations: CD, cesarean delivery; GA, gestational age; ICU, intensive care unit; na, not available; NICU, neonatal intensive care unit.

<sup>a</sup>Danish Medical Birth Register, The Danish Health Data Authority: <https://www.esundhed.dk/Emner/Gravide-foedsler-og-boern/Foedte-og-foedsler-1997-#tabpanel61119A72216248AC86DB508579760DED>. Finnish Birth Registry (<https://thl.fi/en/web/thlfi-en/statistics/statistics-by-topic/sexual-and-reproductive-health/parturients-deliveries-and-births>). Medical Birth Registry of Norway (2018: <http://statistikkbank.fhi.no/mfr/>, 2020: <https://www.fhi.no/hn/helseregistre-og-registre/mfr/svangerskap-og-fodsel-under-koronavirus-pandemien/>). Swedish Medical Birth Registry 2018 (<https://www.socialstyrelsen.se/statistik-och-data/statistik/statistik-forlossningar-och-nyfodda/>). Statistics Iceland: (<http://www.hagstofa.is/>).

<sup>b</sup>Chi-square tests.

<sup>c</sup>Estimate based on total deliveries from March to June 2019 in Denmark, Finland, Iceland; total deliveries from March to June 2020 in Norway and in the Swedish hospitals.

<sup>d</sup>Yangen S *et al.* Maternal deaths in the Nordic countries. *Acta Obstet Gynecol Scand.* 2017;96:1112-1119.

<sup>e</sup>Stillbirth at gestation age  $\geq 22$  weeks or birthweight  $\geq 500$  g.

<sup>f</sup>Neonatal death within 28 days after birth.

## 4 | DISCUSSION

This prospective study in the five Nordic countries showed a low risk of hospital admission due to COVID-19 among pregnant women. Pregnant women hospitalized due to COVID-19 infection were more often obese and more likely to have a migrant background than were women who delivered in 2018. Hospitalization due to COVID-19 was associated with an increased risk of delivering preterm and by cesarean.

We included only women admitted to hospital due to COVID-19 symptoms in the final analyses and excluded women admitted for obstetric reasons, resulting in a study population less influenced by the national testing strategies. These strategies varied over time and between countries during the inclusion period (Figure S1) and could have biased the study results otherwise.

Large population-based cohort studies from the UK and Italy found an incidence of hospitalization with COVID-19 of 2–4.9/1000 maternities,<sup>13–15</sup> which is much higher than the risk of 0.4/1000 deliveries found in Denmark, Finland, Iceland and Norway. However, those studies included admissions for any reason, such as obstetric care and labor. Further, our Nordic study was restricted to women with present infection with a limitation of 14 days between test and admission. Nevertheless, even if all admissions were included in the Nordic countries, the admission risk in Denmark, Finland, Iceland and Norway of 0.8/1000 deliveries was lower than in Italy and the UK. Additionally, the risk of admission was considerably higher in the Swedish regions, which may reflect higher population infection rates and also selection bias, with higher admission rates at university hospitals. The risk of hospital and intensive care admissions in the total population was also higher in Sweden than in the other Nordic countries. This may indicate that policies reducing the transmission in the general population also reduce the risk of hospital admission due to COVID-19 among pregnant women.

Among pregnant women admitted with COVID-19 in the Nordic countries, obesity and migrant background were more common than in the 2018 birth population, corresponding to the findings of previous studies.<sup>9,13,14</sup> This information is relevant when developing national public health strategies.

In the Nordic countries, no maternal, fetal or neonatal deaths were registered among the pregnant women admitted due to COVID-19 during the first 4 months of the pandemic. However, 21% of the women needed intensive care, which is higher than the proportion in previous population-based studies from UK, Italy and the Netherlands,<sup>13,14,23</sup> reflecting our inclusion of only the most severe cases. Previous Swedish and Dutch studies found that pregnant women with COVID-19 had a higher risk of ICU admission compared with non-pregnant women of the same age with COVID-19.<sup>23,24</sup>

Induction of labor, preterm delivery, CD and emergency CD were more frequent among women admitted due to COVID-19 compared with the 2018 birth population, which corresponds to previous findings.<sup>9,13,23</sup> An increasing risk of preterm delivery and CD with increasing severity of COVID-19 has also been reported.<sup>14</sup> A previous study from one of the including Swedish centers found no increased risk of severe outcomes;<sup>25</sup> however, they included COVID-19-positive

women independently of severity or presence of symptoms, which might have biased their results.

Compared with the other Nordic countries, more women admitted to the included hospitals in Sweden had other chronic diseases, which possibly reflects selection bias by inclusion of cases from tertiary care hospitals only. One of the three centers in Sweden implemented universal testing of all obstetric admissions during the inclusion period (Table S1). This is reflected in the higher gestational age at first SARS-CoV-2 test and the shorter interval between test and delivery, since relatively more women with scarce symptoms screened positive upon admission for delivery. Further, fewer women in Sweden than in the other Nordic countries delivered preterm or had a CD, and fewer infants required neonatal care, which reflects the identification of only the most severe cases in the other countries, where different testing strategies were applied.

This study has several strengths. Compared with previous studies, the inclusion of a homogeneous group of pregnant women admitted to hospital because of COVID-19 infection and with a positive test within 14 days of admission, strengthens the assessment of outcomes and controls for variation in testing strategies between the countries. Further, the data were prospectively recorded in medical records and later retrieved, and all reported cases were verified with patient records. Additionally, this study assesses the consequences of COVID-19 by using a comparison group not affected by a pandemic. The Nordic collaboration between several countries with relatively uniform populations provides a larger cohort than would national studies alone, providing relevant data to Nordic and international healthcare providers.

This study also has several limitations. We only reported outcomes for women admitted due to COVID-19 and can therefore not draw conclusions about COVID-19 infection among pregnant women in general. Additionally, the aggregate data currently available did not allow for assessment of individual risk factors and mediating factors. Prospective reporting could potentially cause underreporting of cases by lack of identification. Assessment of completeness by linkage to the National Infectious Disease and the Medical Birth Registry was done in Denmark and Iceland, but was not yet possible in the other countries. However, the number of cases in Denmark was comparable to numbers in Finland, Iceland and Norway, where testing strategies were similar, indicating that most cases were identified. The Swedish data represent three large tertiary centers, equivalent to 22% of the annual deliveries in Sweden, and there is a potential risk for both underreporting and selection bias in the Sweden data. We therefore presented data for all countries combined and for Denmark, Iceland, Finland and Norway alone.

We did not have concurrent data for non-infected pregnancies available for comparison at the time of publication. We therefore relate the results to 2018 data not influenced by the pandemic, which may be viewed as an advantage. However, the NOSS COVID-19 group plans to analyze data against population data for 2020 when it is released from the Nordic Medical Birth Registries.

Studies similar to the NOSS COVID-19 collaboration are taking place in several countries worldwide as part of the International

Network of Obstetric Survey Systems (INOSS).<sup>25</sup> Uniform international population-based studies are needed to reduce potential selection bias in institution-based studies. Combining data internationally will allow assessment of rare, severe complications and risk factors, and aid in the understanding of the disease in pregnancy even better.

## 5 | CONCLUSION

This multinational Nordic study showed a low risk of admission due to COVID-19 in pregnancy in the Nordic countries. Women admitted to hospital due to COVID-19 were more frequently obese or had a migrant background compared with non-infected women. A fifth of the admitted women required intensive care and we observed higher risks of preterm and cesarean deliveries than among deliveries in 2018. The study indicates that the risk of admission and complications in pregnancy related to COVID-19 may be associated with national public health measures to reduce transmission of disease.

The Nordic collaboration is important in collecting robust data and may provide future benefits in the analysis of rare obstetric outcomes in pandemic responses.

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## AUTHOR CONTRIBUTIONS

All authors participated in the joint study planning and in planning and implementing their respective national data collection. HE, AA, TS, EJ and OÅ summarized the national datasets. HE, AA and KK analyzed the data. HE and AA drafted the manuscript and amended it according to feedback from all authors.

## CONFLICT OF INTEREST

None.

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## SUPPORTING INFORMATION

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

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