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SARS-CoV-2 infection among hospitalized pregnant women and impact of different viral strains on COVID-19 severity in Italy: a national prospective population-based cohort study

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Abstract

Objective The primary aim of this paper was to describe SARS-CoV-2 infection among pregnant women during the Wild-type and the Alpha period in Italy, the secondary aim was to compare the impact of the virus variants on the severity of maternal and perinatal outcomes.

Design National population-based prospective cohort study.

Setting 315 Italian maternity hospitals.

Sample 3,306 women with SARS-CoV-2 infection confirmed within 7 days from hospital admission.

Methods Cases were prospectively reported by trained clinicians for each participating maternity unit. Data were described by uni and multivariate analysis.

Main outcome measures COVID-19 pneumonia, ventilatory support, intensive care unit (ICU) admission, mode of delivery, preterm birth, stillbirth, maternal and neonatal mortality.

Results 64.3% of the cohort was asymptomatic, 12.8% developed a COVID-19 pneumonia and 3.3% required ventilatory support and/or ICU admission. Maternal age of 30-34 years (OR 1.43, 95% CI 1.09-1.87) and ≥35 (1.62, 1.23-2.13), citizenship from High Migration Pressure Countries (1.75, 1.36-2.25), previous comorbidities (1.49, 1.13-1.98) and obesity (1.72, 1.29-2.27) were associated with higher pneumonia occurrence. Preterm birth rate was 11.1%. In comparison with the pre-pandemic period, stillbirths, maternal and neonatal deaths remained stable. The need for ventilatory support and/or ICU admission among women with pneumonia increased during the Alpha compared to the Wild-type period (3.24, 1.99-5.28).

Conclusions Our results are consistent with low risk of severe COVID-19 disease among pregnant women and rare adverse perinatal outcomes. During the Alpha variant period, there was a significant increase of severe COVID-19 illness. Further research is needed to describe the impact of different SARS-CoV-2 viral strains on maternal and perinatal outcomes.

Keywords cohort studies, Italy, pregnancy, SARS-CoV-2, COVID-19 pneumonia.

Tweetable abstract the rate of severe COVID-19 disease increased during the Alpha compared to the Wild-type period.

Introduction

A two-wave pattern of the COVID-19 disease during the 2020 pandemic infection was observed in Italy with the first wave during spring followed by the second wave starting during autumn and extending until the end of June 2021.

Following the unexpected onset of the pandemic at the end of February, the Italian Government imposed a lockdown lasting from 9th March to 18th of May. During the summer, there was greater social interaction all over the country, despite the maintenance of mandatory preventive measures such as safe interpersonal distancing and face mask protection. Towards the end of August, the virus began to re-circulate, and, in the fall, a second wave occurred, affecting central and southern Italy, which had previously been spared.

Since February 2021, rapid investigations sequencing and analysing the genetic code of a significant number of positive samples at national level, allowed to monitor the circulation of SARS-CoV-2 variants.[1] In February and March 2021 the estimated national prevalence of the Alpha variant was respectively 54%[2] and 86.7%.[3]

From mid-June, thanks to the reduced circulation of the virus the restrictions were decreased. The Delta variant began to take over in mid-June when a prevalence of 22.7% was detected.[4] Although estimates are not available for pregnant women, it is reasonable to imagine a similar trend for this population.

Data from UK suggest that the Alpha and Delta variants have a worse impact on maternal and perinatal outcomes.[5,6] Research capable of gathering sound information on the impact of different SARS-CoV-2 variants in pregnancy is therefore urgently needed to guide decision-makers, support health professionals and inform citizens.

From the beginning of the pandemic, the Italian Obstetric Surveillance System (ItOSS) launched a national population-based prospective study enrolling any pregnant woman with confirmed SARS-CoV-2 infection, admitted to hospital until the end of June 2021.[7-9] ItOSS coordinates public health research in the obstetric field in Italy through an enhanced maternal mortality surveillance system,[10] and coordinates prospective population-based studies on severe maternal morbidity,[11-13] in collaboration with the multi-country International Network of Obstetric Survey System (INOSS).[14]

The primary aim of this paper was to describe SARS-CoV-2 infection among pregnant women during the Wild-type period and the Alpha period in Italy, the secondary aim was to compare the impact of the virus variants on the severity of maternal and perinatal outcomes.

Methods

This national population-based prospective cohort study collects information on women with confirmed SARS-CoV-2 infection, admitted to any Italian hospital during pregnancy and up to 42 days after childbirth.

All Italian maternity hospitals that managed SARS-CoV-2 positive women were invited to participate in the project. Trained reference clinicians notified eligible women and collected comprehensive information on maternal socio-demographic characteristics, medical and obstetric history, disease management, mode of delivery and maternal and perinatal outcomes, through a dedicated online form that was revised and pre-tested by a multidisciplinary national group of experts. Weekly email reminders and phone contacts ensured complete reporting from the participating reference clinicians.

Confirmed SARS-CoV-2 infection was defined as the detection of viral RNA on reverse transcriptase-polymerase chain reaction (RT-PCR) testing of nasopharyngeal swab and/or blood and/or the radiological diagnosis of COVID-19 pneumonia. Until the end of March 2020, only symptomatic pregnant women and those defined as close contacts of a SARS-CoV-2 infected person were tested. In April, the Italian Regions progressively adopted universal screening policies during pregnancy. Therefore, from May 2020, all pregnant women admitted to hospital were tested for SARS-CoV-2, regardless of symptoms or exposure.

The present analysis refers to pregnant women with confirmed SARS-CoV-2 infection detected within 7 days from hospital admission during the Wild-type and the Alpha period, defined respectively as the period between February 25, 2020 and January 31, 2021, and between February 1 and June 30, 2021. The cases of the first period, for which complete data have been received by June 30, 2021, are consolidated, while reference clinicians are still adding cases to the Alpha period.

Outcomes

Outcome measures included in the study are: COVID-19 pneumonia confirmed by chest imaging, mechanical ventilatory support (non-invasive mechanical ventilation, orotracheal intubation, extracorporeal membrane oxygenation (ECMO)), intensive care unit (ICU) admission, maternal mortality (maternal death during pregnancy or within 42 days from any pregnancy outcome), preterm birth (divided in 22-31 and 32-36 gestational weeks), mode of delivery (vaginal, elective caesarean section (CS), urgent/emergency CS due to COVID-19, urgent/emergency CS due to maternal/foetal indications), stillbirth (intrauterine foetal death ≥22 completed weeks of gestation), neonatal intensive care unit (NICU) admission, early neonatal mortality (death of a live-born infant <7 days of life).

Covariates

Covariates include socio-demographic and medical characteristics that could act as potential risk factors: age (<30, 30-34, and ≥35 years), citizenship (Italian, citizenship from High Migration Pressure Countries (HMPC), citizenship from other countries),[15] educational level (low: primary school or lower; medium: high school; high: bachelor's degree or higher), previous comorbidities (at least one of the following: diabetes, asthma requiring medical treatment, hypertension, cardiovascular diseases, lung diseases, HIV/AIDS, other pathologies), obesity (body mass index (BMI)>30 kg/m^2).

Statistical analysis

Statistical analyses were performed using the Statistical Package STATA/MP version 14.2. Frequency distributions, prevalence and odds ratios (ORs) with their 95% confidence intervals (CI) were used to describe data. Missing data were excluded when their proportion was lower than 5%, otherwise they were included in the frequency distributions.

The national SARS-CoV-2 incidence rate in pregnancy with 95% CI was estimated for the two considered periods. All enrolled women with ongoing pregnancies or who gave birth, irrespective of time of diagnosis, were included in the numerator. The 2019 deliveries retrieved from the national Birth Registry[16] were used to estimate the denominators, applying variations corresponding to the Italian National Statistics Institute (ISTAT) estimate of births reduction observed between 2019 and the corresponding months of the two study periods.[17] Finally, deliveries were weighted according to the computed time of exposure to risk of infection during pregnancy.

Frequency distributions by socio-demographic, obstetric and medical characteristics were computed for the two periods. Prevalence of COVID-19 pneumonia, its risk factors and its trend during the study period were analysed. The Birth Register data were used as background population to compare the ItOSS prevalence of foreign women, caesarean sections and preterm births with the 2019 national data.

To assess the association between presence/absence of pneumonia and its potential risk factors (woman's age, citizenship, educational level, presence/absence of previous comorbidities, presence/absence of obesity), mutually adjusted ORs and their 95% CI were calculated using a multiple logistic regression model. Plausible interactions were tested using the Likelihood Ratio Test. To account for missing information, the model was applied to multiple-imputed data (Appendix S1, Table S1). Imputation of 20 datasets was performed using chained equations;[18] Rubin's rules were used to combine model's estimates across the 20 datasets.[19] The model was also performed using only complete cases as sensitivity analysis (Table S2).

To compare the impact of the Alpha variant vs the Wild-type on maternal and perinatal outcomes, the prevalence of need for ventilatory support and ICU admission were described among women with pneumonia during the two periods. A logistic regression model was applied to estimate ORs

and their 95% CI for ventilatory support and/or ICU admission, using the first period as reference. ORs were adjusted for woman's age, citizenship, previous comorbidities and obesity. Severe outcomes (ICU admission, orotracheal intubation and maternal deaths) were compared to those recorded among the background population of hospitalized positive women aged 15-49 years.[20] Mode of delivery, gestational age at delivery, and perinatal outcomes were analysed stratified by the presence/absence of COVID-19 pneumonia. Maternal deaths were cross-checked with the ItOSS enhanced maternal mortality surveillance system.[21]

In this observational study, no formal power calculation was performed because the sample size was governed by the disease incidence.

Results

All the 315 Italian maternity units (Appendix S2) invited have participated in the study (100% attendance rate), notifying 5,734 women with confirmed SARS-CoV-2 infection during pregnancy and up to 42 days after childbirth from February 25, 2020 to June 30, 2021. The flow diagram in Figure 1 describes the selection of the cases included in the present analysis, represented by 3,306 women with a positive SARS-CoV-2 test within 7 days from hospital admission, with ongoing pregnancy or who gave birth, during the Wild-type (n=2,550) and the Alpha period (n=756).

The national SARS-CoV-2 incidence rate estimated among the ItOSS cohort of pregnant women was respectively 20.1 per 1,000 births (95% CI 19.4-20.7) during the Wild-type period, and 14.9 per 1,000 (95% CI 14.2-15.6) during the Alpha period.

Table 1 describes the characteristics of the enrolled women during the two considered periods. The socio-demographic characteristics do not differ between the Wild-type and Alpha period. The percentage of women of foreign citizenship was significantly higher compared to women who gave birth in 2019 in Italy.[15] At the first positive SARS-CoV-2 test, the great majority (92.9%) of women was in the third trimester of gestation. The main reason for the admission to the hospital was the COVID-19 infection disease (57.6%) for women with ongoing pregnancy (13.6%) while other obstetric reasons or labour and delivery (82.7%) were main causes for hospitalization of those who gave birth (86.4%) (Table S3). Out of the 3,306 women, 64.3% was asymptomatic at diagnosis whereas 12.8% developed COVID-19 pneumonia, of which 40.9% among women with ongoing pregnancy and 8.4% among those who gave birth.

Age between 30 and 34 years (OR 1.43, 95% CI 1.09-1.87) and ≥35 years (OR 1.62, 95% CI 1.23-2.13), citizenship from HMPCs (OR 1.75, 95% CI 1.36-2.25), previous comorbidities (OR 1.49, 95% CI 1.13-1.98) and obesity (OR 1.72, 95% CI 1.29-2.27) were significantly associated to higher COVID-19 pneumonia occurrence. No statistically significant association was found with educational level. Results did not noticeably change in the sensitivity analysis (Table S2).

Table 2 describes maternal and perinatal outcomes stratified by the presence/absence of COVID-19 pneumonia during the two periods. Overall, 3.3% of the women developed severe COVID-19 pneumonia requiring mechanical ventilatory support and/or ICU admission. A significant increase in resort to ventilatory support and/or ICU admission in case of pneumonia was observed during the Alpha period, compared to the Wild-type (OR adjusted for age, citizenship, previous comorbidities and obesity was 3.24, 95% CI 1.99-5.28). Except for maternal deaths, the outcomes shown in Table 2 worsened during the period characterized by the circulation of the Alpha variant. In comparison to the background population of hospitalized positive women aged 15-49 years,[20] the percentage of women undergoing orotracheal intubation was slightly higher (1.1% vs 0.7%), and the admission to ICU and mortality were lower among the ItOSS cohort (respectively 2.3% vs 5.5% and 0.03% vs 1.3%).

Overall, 11.6% of 2,888 livebirths was admitted to NICU, with the highest prevalence among those delivered by mothers with pneumonia (27.1%) compared to those delivered by unaffected women (10.1%). NICU admissions increased from 25.7% during the Wild-type period to 30.0% during the Alpha period (Table 2). Stillbirths (0.7%) and early neonatal deaths (0.2%) were not associated to maternal pneumonia, nor to the different viral strains. The national stillbirth rate registered in the first semester of 2020 (2.82/1,000) was in line with those recorded during the previous four years (ranging from 2.59/1,000 in 2018 to 2.86/1,000 in 2015).[22]

Table 3 shows mode of delivery and gestational age at birth among 2,856 women who gave birth. Overall, the CS rate (34.1%) remained close to the 2019 national figure (31.8%).[16] Urgent/emergency CS due to COVID-19 was steadily higher among women affected by COVID-19 pneumonia (20.4%) compared to 0.4% of the unaffected ($p < 0.001$); during the Alpha period, the proportion rose to 31.2% in case of pneumonia.

The proportion of preterm births (11.1%), mostly late preterm, was higher compared to the 2019 national figure (6.7%).[16] Among women with COVID-19 pneumonia, the preterm birth rate was significantly higher compared to the unaffected ($p < 0.001$), reaching 43.4% during the Alpha period (OR adjusted for age, citizenship, previous comorbidities and obesity, compared to the Wild-type first period, was1.69, 95% CI 0.94-3.04). Iatrogenic indications, defined as elective CS or induction of labour, accounted for 27.2% of the preterm births.

Discussion

Main findings

From February 2020 to June 2021, the ItOSS prospective population-based national cohort study enrolled 3,306 pregnant women with confirmed SARS-CoV-2 infection within 7 days from hospital

admission. At time of diagnosis, 64.3% of the cohort was asymptomatic, while COVID-19 pneumonia affected 12.8% of the women. ICU admission and maternal mortality among the ItOSS cohort were lower compared to the same figures detected among the background population of infected women aged 15-49 years.[20] Overall, 3.3% needed mechanical ventilatory support and/or ICU admission. During the Alpha period, the need of ventilatory support and/or ICU admission among women affected by COVID-19 pneumonia was two times the Wild-type period. Compared to the pre-pandemic period, the rate of stillbirths and maternal and neonatal deaths remained stable.[22] Altogether our results showed an absolute low risk of severe adverse outcomes.

Strengths and limitations

The national prospective population-based design, the presence of trained clinicians in each hospital and the active monitoring of case reporting through monthly checks are among the main strengths of the study. Thanks to routine testing for SARS-CoV-2 from May 2020, the data analysis relayed on a complete denominator, which significantly improved the accuracy of outcomes measures. The ItOSS data were able to distinguish hospital admissions for COVID-related circumstances from those related to delivery or other obstetric conditions, thus favouring the interpretation of the observed different clinical patterns among women with ongoing pregnancy and those who gave birth. Data analysis by pneumonia status allowed better description of risk factors and characteristics of women at higher risk for adverse outcomes. Moreover, the inclusion in the analysis of pregnant women with a confirmed positive test within 7 days from hospital admission limited possible selection bias. The crosscheck of the mortality data with the ItOSS enhanced maternal mortality surveillance is a further strength of the study. The limitations of the study include the unavailability of a control population, and the likely missing cases of SARS-CoV-2 positive women before May 2020 when universal testing started. The lack of a data crosscheck with the national SARS-CoV-2 surveillance that does not collect information about pregnant women is a further limitation. Due to pending completion of pregnancy for all women enrolled in the cohort and due to incomplete data of the second pandemic wave, findings are not conclusive.

Interpretation

Similarly to ItOSS, during the Wild-type period the United Kingdom Obstetric Surveillance System (UKOSS)[23,24] and the Nordic Obstetric Surveillance Study (NOSS)[25] prospective population-based studies detected an absolute low risk for hospital admission of SARS-CoV-2 pregnant women due to COVID-19 severe disease, and no increase in stillbirth rate and maternal and neonatal deaths. On the contrary, the Centers for Disease Control and Prevention (CDC) passive surveillance[26] and the following meta-analysis mainly built on CDC report,[27] described a higher prevalence of COVID-19 severe disease among pregnant women and poor maternal and perinatal outcomes compared to the

ItOSS results. These differences seem to be mostly related to the adopted study design. For instance, the retrospective passive CDC surveillance[26] was affected by 64.5% missing data on pregnancy status, compared to the complete reporting of the prospective population-based studies launched in the countries participating in the INOSS.[14]

The multinational INTERCOVID study reported a 22-fold higher risk for maternal mortality among SARS-CoV-2 positive pregnant women.[28] However, all deaths were detected in low-income countries, probably as a consequence when conditions became critical. The different impact of the pandemic observed between high and low-resource settings, in fact, requires caution in inferring detected unfavourable outcomes.

As reported by other studies,[23-28] we confirmed that obese women and those with previous comorbidities were more likely to develop severe COVID-19 disease. Pregnant women from HMPCs were also significantly more likely to be hospitalized with severe pneumonia, probably due to lower socioeconomic status and possible delay in accessing health services.

Regarding the increased risk of preterm births, after excluding all cases with iatrogenic indications (27.2% of preterm births), the rate of spontaneous preterm births dropped to 8.1%, much closer to the 2019 national figure of 6.7%.[16] However, the increase in preterm births detected during the Alpha period confirms the UKOSS data[6] and urges a careful evaluation of the impact of new variants on perinatal outcomes. Luckily, as reported by UKOSS,[24] preterm babies were late pre-term more likely to be admitted to NICU without any increase in stillbirths and neonatal deaths.

Unexpectedly, we did not record a significant increase in CS as reported in many systematic reviews,[27,29,30] in the UK[23,24] and Northern Europe[25] where usually CS rates are lower compared to Italy. The ItOSS detected a higher rate of CS only among women affected by COVID-19 pneumonia, while the increase reported by UKOSS is irrespective of symptom status.[21] The great effort to inform Italian obstetricians that COVID-19 was not a primary indication for CS,[28-29] flanked by the study monitoring and periodic return of preliminary data, probably helped limit CS. During the first weeks from the pandemic outbreak, the Istituto Superiore di Sanità (Italian National Institute of Health, ISS) published a weekly report to describe new evidence on SARS-CoV-2 infection among pregnant women in support of clinicians, and an average of 7.500 health professionals accessed the website daily.[31] Moreover, the virus circulated more in the North of the country, which has a lower CS rate compared to southern Italy.[16] A previous ItOSS paper described in detail the procedures and criticalities of peripartum care during the first pandemic wave in Italy.[9]

The lower SARS-CoV-2 incidence rate detected during the Alpha compared to the Wild-type period, is likely due to the start of the vaccination campaign. In Italy the vaccine was primarily indicated for

pregnant women at high risk of viral exposure (i.e. healthcare providers, caregivers) or with underlying conditions that increase the risk of severe COVID-19.[33]

During the Alpha compared to the Wild-type period we detected a significant increase in resort to ventilatory support and/or ICU admission in case of pneumonia. On the contrary, maternal mortality as well as perinatal morbidity and mortality have not worsened. Similar figures have been reported by UK during the second pandemic wave, assuming a possible association with the emergence of the Alpha variant described as a more pathogenic strain of SARS-CoV-2.[3] The ItOSS data seem to confirm this hypothesis, since about 85% of circulating viruses in Italy were replaced by the Alpha variant in mid-March 2021[3] and the comparison of women's socio-demographic and obstetric characteristics during the two periods do not show any significant difference in support of the worse outcomes observed during the Alpha period. Clinicians should be therefore aware that the emergence of new viral strains could be related to more severe illness as described by the recent UKOSS paper for the Alpha and the Delta viral strains. [6]

Conclusion

Further research able to correlate viral sequencing with epidemiological data is needed to confirm whether variants of the SARS-CoV-2 virus may be responsible for worse maternal and perinatal outcomes. The level of circulation of the virus, and the emergence of new viral strains with increased transmissibility and/or virulence are aspects to be taken into consideration when defining public health indications, as in the case of vaccination during pregnancy. For instance, the Italian Ministry of Health and the ISS updated the *interim* indications on COVID-19 vaccination during pregnancy[33] as a result of worse maternal outcomes detected during the Alpha period by the ItOSS project. The vaccine, originally recommended only for pregnant women at higher risk of SARS-CoV-2 exposure or morbidity, is now recommended for all pregnant women starting from the second trimester.[34]

During the SARS-CoV-2 emergency, non-population-based series at risk of duplication of the same cases and without appropriate denominators as well as the publication of systematic reviews affected by the low quality of the available observational studies, and the premature media coverage of preprints, challenged the research responsiveness. Future research should address the need to balance speed with accuracy in producing knowledge during pandemic outbreaks.

Disclosure of interests

The authors declare no conflict of interests. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

conceived the

study and provided overall guidance

SD conceived the study, provided overall guidance, drafted the manuscript and reviewed the final version. EC collected data, collaborated to draft the manuscript, edited and reviewed the final version. Alice Maraschini and MAS conducted the statistical analysis, assisted with data collection, collaborated to draft the manuscript and reviewed the final version. RB, MDM and MF collaborated to statistical analysis. MAA, RB, AC, PC, IC, LC, GD, EDA, SDE, GE, MPF, LL, Marco Liberati, Mariavittoria Locci, ALR, CM, GM, FM, Alessandra Meloni, ADM, LM, EP, LP, LR, AS, VS, SCAS, GS, DS, SS, MS, FT, ST, VT, CT, AV supervised, assisted with data collection and reviewed the final version. All authors have read and agreed to the published version of the manuscript.

Details of ethics approval

The Ethics Committee of the INHI approved the project (Prot. 0010482 CE 01.00, Rome 24/03/2020). The study protocol is available at: https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-pregnancy-childbirth-breastfeeding-prospective-study-itoss (Italian).

An informed consent to participate to the study was acquired from any woman at study enrolment.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. Multiple imputation

Appendix S2. The ItOSS national network of maternity units

Table S1. Differences between women with and without missing data on educational level

Table S2. COVID-19 pneumonia mutually adjusted odds ratios - Logistic regression model applied to complete cases

Table S3. Reasons for hospital admission

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Table/Figure Caption List

Figure 1. Women enrolled in the ItOSS cohort during the Wild-type (Feb 25, 2020 – Jan 31, 2021) and Alpha period (Feb 1 – Jun 30, 2021)

Table 1. Women's characteristics during the Wild-type (Feb 25, 2020 – Jan 31, 2021) and Alpha period (Feb 1 – Jun 30, 2021)

Table 2. Women's and perinatal outcomes

Table 3. Mode of delivery and gestational age at birth

Table 1. Women's characteristics during the Wild-type (Feb 25, 2020 – Jan 31, 2021) and Alpha period (Feb 1 – Jun 30, 2021)

	25/2/2020-31/1/2021 (n=2,550)		**1/2-30/6/2021** (n=756)		**Total** (N=3,306)	
	n	**%**	**n**	**%**	**n**	**%**
Age, years (56 missing):						
<30	883	35.2	242	32.8	1125	34.6
30-34	856	34.1	273	37.0	1129	34.7
≥35	773	30.8	223	30.2	996	30.6
Citizenship:						
Italian	1792	70.3	544	72.0	2336	70.7
HMPCs	752	29.5	210	27.8	962	29.1
Non-HMPCs	6	0.2	2	0.3	8	0.2
Country of birth:						
Italy, Western Europe and North America	1640	64.3	517	68.4	2157	65.2
East Europe	232	9.1	97	12.8	329	10.0
Africa	349	13.7	76	10.1	425	12.9
South/Central America	138	5.4	26	3.4	164	5.0
Asia	191	7.5	40	5.3	231	7.0
Level of education:						
Low	555	21.8	175	23.1	730	22.1
Medium	784	30.7	248	32.8	1032	31.2
High	411	16.1	133	17.6	544	16.5
Missing	800	31.4	200	26.5	1000	30.2
Previous comorbidities (90 missing)	325	13.0	89	12.4	414	12.9
Pre-gestational diabetes	58	2.3	15	2.1	73	2.3
Autoimmune disease	46	1.8	17	2.4	63	2.0
Chronic hypertension	38	1.5	7	1.0	45	1.4
BMI>30 kg/m^2 (71 missing)	328	13.1	99	13.4	427	13.2
Multiparous (18 missing)	1399	55.2	436	57.9	1835	55.8
Multiple pregnancy (1 missing)	12	2.2	54	2.0	66	2.0
Gestational age at diagnosis, weeks (55 missing):						

≤14	35	1.4	5	0.7	40	1.2
15-27	145	5.8	45	6.1	190	5.8
≥28	2336	92.8	685	93.2	3021	92.9
Presence of COVID-19 pneumonia	299	11.7	125	16.5	424	12.8
Asymptomatic women (33 missing)	1652	65.3	454	61.2	2106	64.3
Ongoing pregnancy	338	13.3	112	14.8	450	13.6

HMPCs: high migration pressure countries

BMI: body mass index

Table 2. Women's and perinatal outcomes

Women's outcome	**25/2/2020-31/1/2021**				**1/2-30/6/2021**			
	No COVID-19 pneumonia (n=2,251)		**COVID-19 pneumonia** (n=299)		**No COVID-19 pneumonia** (n=631)		**COVID-19 pneumonia** (n=125)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Oxygen therapy	21	0.9	158	52.8	24	3.8	92	73.6
Mechanical ventilatory support and/or ICU admission	0	0.0	56	18.7	0	0.0	52	41.6
Non-invasive ventilatory support	0	0.0	53	17.7	0	0.0	47	37.6
Invasive ventilatory support:	0	0.0	15	5.0	0	0.0	21	16.8
Orotracheal intubation	0	0.0	14	4.7	0	0.0	21	16.8
ECMO	0	0.0	3	1.0	0	0.0	4	3.2
ICU admission	0	0.0	35	11.7	0	0.0	40	32.0
Death	0	0.0	1	0.3	0	0.0	0	0.0
Perinatal outcome	n=2,081		n=169		n=578		n=80	
Stillbirth	15	0.7	2	1.2	3	0.5	0	0.0
Livebirth	2066	99.3	167	98.8	575	99.5	80	100.0
Neonatal death	3	0.1	1	0.6	2	0.3	1	1.3
NICU admission	212	10.3	43	25.7	55	9.6	24	30.0

ICU: intensive care unit

ECMO: extracorporeal membrane oxygenation

NICU: neonatal intensive care unit

Table 3. Mode of delivery and gestational age at birth

	25/2/2020-31/1/2021				1/2-30/6/2021			
	No COVID-19 pneumonia (n=2,049)		COVID-19 pneumonia (n=163)		No COVID-19 pneumonia (n=567)		COVID-19 pneumonia (n=77)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Mode of delivery (8 missing):								
Vaginal	1381	67.6	74	46.0	399	70.4	23	29.9
Elective CS	315	15.4	19	11.8	84	14.8	8	10.4
Urgent/emergency CS due to maternal/foetal indication	337	16.5	43	26.7	84	14.8	22	28.6
Urgent/emergency CS due to COVID-19	10	0.5	25	15.5	0	0.0	24	31.2
Gestational age at birth, weeks (51 missing):								
≤31	31	1.5	16	10.3	9	1.6	8	10.4
32-36	146	7.2	38	24.4	39	6.9	25	32.5
≥37	1847	91.3	102	65.4	501	88.4	43	55.8
Missing	1381	67.6	74	46.0	18	3.2	1	1.3

CS: caesarean section

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