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Journal of Gynecology Obstetrics and Human Reproduction 49 (2020) 101826

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Original Article

A snapshot of the Covid-19 pandemic among pregnant women in France

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ARTICLE INFO

Article history:
Received 29 May 2020
Accepted 31 May 2020
Available online 4 June 2020

Keywords:
COVID 19
Respiratory complications
Risk factors
Lockdown

ABSTRACT

Objective: To describe the course over time of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in French women from the beginning of the pandemic until mid-April, the risk profile of women with respiratory complications, and short-term pregnancy outcomes.
Methods: We collected a case series of pregnant women with COVID-19 in a research network of 33 French maternity units between March 1 and April 14, 2020. All cases of SARS-CoV-2 infection confirmed by a positive result on real-time reverse transcriptase polymerase chain reaction tests of a nasal sample and/or diagnosed by a computed tomography chest scan were included and analyzed. The primary outcome measures were COVID-19 requiring oxygen (oxygen therapy or noninvasive ventilation) and critical COVID-19 (requiring invasive mechanical ventilation or extracorporeal membrane oxygenation, ECMO). Demographic data, baseline comorbidities, and pregnancy outcomes were also collected.
Results: Active cases of COVID-19 increased exponentially during March 1–31, 2020; the numbers fell during April 1–14, after lockdown was imposed on March 17. The shape of the curve of active critical

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http://dx.doi.org/10.1016/j.jogoh.2020.101826

COVID-19 mirrored that of all active cases. By April 14, among the 617 pregnant women with COVID-19, 93 women (15.1 %; 95 %CI 12.3–18.1) had required oxygen therapy and 35 others (5.7 %; 95 %CI 4.0–7.8) had had a critical form of COVID-19. The severity of the disease was associated with age older than 35 years and obesity, as well as preexisting diabetes, previous preeclampsia, and gestational hypertension or preeclampsia. One woman with critical COVID-19 died (0.2 %; 95 %CI 0−0.9). Among the women who gave birth, rates of preterm birth in women with non-severe, oxygen-requiring, and critical COVID-19 were 13/123 (10.6 %), 14/29 (48.3 %), and 23/29 (79.3 %) before 37 weeks and 3/123 (2.4 %), 4/29 (13.8 %), and 14/29 (48.3 %) before 32 weeks, respectively. One neonate (0.5 %; 95 %CI 0.01–2.9) in the critical group died from prematurity.

Conclusion: COVID-19 can be responsible for significant rates of severe acute, potentially deadly, respiratory distress syndromes. The most vulnerable pregnant women, those with comorbidities, may benefit particularly from prevention measures such as a lockdown.

Introduction

The pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), hit France in early March 2020; lockdown was imposed on March 17. COVID-19's consequences in pregnant women are poorly documented [1–4], few maternal complications have been reported, and most information so far comes from China [1–4]. For now, the absence of comparisons with appropriate controls means we cannot know whether pregnant women are at higher risk of developing severe complications than the general population [3,4]. Their risk factors for respiratory complications are suggested to mirror those in the general population [5,6].

There is however no data from a large series about the general and obstetric risk factors for developing respiratory complications, especially critical COVID-19 or about the obstetric consequences of these complications. We therefore undertook a national survey with a follow-up ending on April 14, 2020, through a French research network: the Groupe de Recherche en Obstétrique et Gynécologie (GROG).

Our main objectives were to describe the course over time of SARS-CoV-2 infection in French pregnant women, the clinical profile and risk factors for women with maternal respiratory complications, and short-term pregnancy outcomes.

Methods

This case series came from a research network of 33 French maternity units (including 24 tertiary referral centers representing around 114 000 deliveries annually, 15 % of French births). Aggregated data, extracted from medical files by local physicians, from all diagnosed cases of COVID-19 in pregnant women in these hospitals (for prenatal care, illness, or delivery) from March 1 to April 14 were merged and analyzed to provide a snapshot of the pandemic's consequences in this population. During this period, the French health authorities recommended diagnostic tests only in women with symptoms or diagnosed contacts [7]. Infections were diagnosed by the real-time reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2 nucleic acid (from nasal swabs) and/or a computed tomography (CT) chest scan. Women were considered, as proposed by French health authorities [7], to have recovered from COVID-19 if, 10 days after diagnosis or 14 days after symptoms began, they were asymptomatic for more than 48 h. Otherwise, COVID-19 cases were considered active.

We first describe the temporal trends of COVID-19, the reasons for and the gestational age at diagnosis, as well as COVID-19 respiratory complications in the overall population. We then report maternal characteristics and maternal, pregnancy, and neonatal outcomes according to the severity of the respiratory disease, categorized in 3 exclusive groups: non-severe (no respiratory support), requiring oxygen (nasal oxygen therapy or noninvasive ventilation), or critical (invasive mechanical ventilation or extracorporeal membrane oxygenation, ECMO).

Maternal and neonatal characteristics and outcomes were described as frequencies and percentages. Linear trends of categorical variables were tested by the Chi-squared trend test developed by Royston [8]. Differences between women with non-severe COVID-19 and those with any respiratory support (oxygen-requiring and critical) were expressed as risk ratios (RR) with their 95 % confidence intervals (CI). Data were analyzed with Stata/SE 13.0 (StataCorp LP, College Station, Texas). This study received IRB approval (CEROG 2020-OBST-0403).

Results

Active cases of COVID-19 increased exponentially during the entire month of March; the numbers fell during April 1–14 (Fig. 1A), after the imposition of lockdown, on March 17. The shape of the curve of active critical COVID-19 cases mirrored that of all active cases (Fig. 1B).

By April 14, 617 pregnant women in the 33 participating centers had been diagnosed with COVID-19, and 497 (80.6 %) of them were symptomatic (Table 1). The most frequent symptoms leading to diagnosis were cough, fever, anosmia, and dyspnea. Shortness of breath led to nasal oxygen therapy for 83 women, noninvasive ventilation for 10, invasive mechanical ventilation for 29, and ECMO for 6 (Table 1). Therefore, 93 (15.1 %; 95 %CI 12.3–18.1) women required oxygen therapy and 35 (5.7 %; 95 %CI 4.0–7.8) had a critical form of COVID-19.

The severity of the disease was associated with age over 35 and obesity, as well as preexisting diabetes, previous preeclampsia, and gestational hypertension or preeclampsia (Table 2). One woman with critical COVID-19 died (0.2 %; 95 %CI 0.004−0.9).

By April 14, 486 (78.8 %) women had recovered from COVID-19, and 123/489 (25.1 %) in the non-severe group, 29/93 (31.2 %) requiring oxygen, and 29/35 (85.3 %) in the critical group (P for trends <0.001) had given birth. Among the 181 (29.3 %) women who gave birth, rates of prematurity before 37 weeks were 13/123 (10.6 %), 14/29 (48.3 %), and 23/29 (79.3 %) in women with non-severe, oxygen-requiring and critical COVID-19, respectively, and before 32 weeks, 3/123 (2.4 %), 4/29 (13.8 %), 14/29 (48.3 %). Rates of cesarean for COVID-19 symptoms and of admission to neonatal intensive care unit increased with severity. Two (1.1 %; 95 %CI 0.1–3.8) neonates had positive SARS-CoV-2 RT-PCR. There was one (0.5 %; 95 %CI 0.01–2.9) neonatal death in the critical group due to prematurity.

Discussion

Initial reports of COVID-19 during pregnancy did not describe any serious maternal or neonatal complications [1–4]. In this large

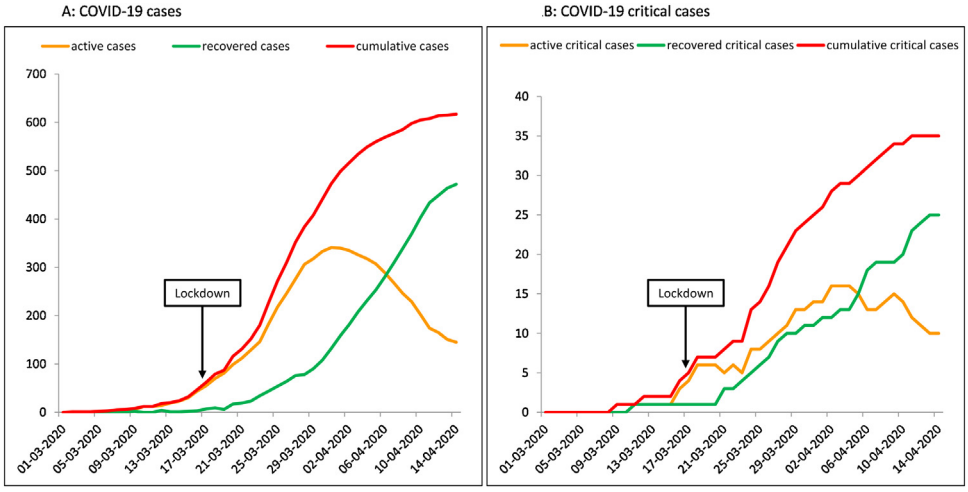

Fig. 1. Temporal trends of COVID-19 cases in pregnant women in France.

Table 1
Diagnosis and COVID-19 severity among pregnant women in France.

	Pregnant women with COVID-19 N = 617
Reasons for diagnosis*	
Cough	384 (62.2)
Fever	285 (46.2)
Anosmia	172 (27.9)
Dyspnea	165 (26.7)
Diarrhea	54 (8.8)
Other minor symptoms	124 (20.1)
Positive contact person	115 (18.6)
Systematic	5 (0.8)
Mode of diagnosis*	
Positive RT-PCR	597 (96.8)
Chest CT typical features	51 (8.3)
Gestational age at diagnosis	
14–21 wk	105 (17.0)
22–31 wk	238 (38.6)
32–36 wk	142 (23.0)
≥ 37 wk and post-partum period	132 (21.4)
Hospitalization	253 (41.0)
Respiratory support	128 (20.7)
Nasal oxygen therapy	83 (13.5)
Noninvasive ventilation	10 (1.6)
Invasive mechanical ventilation	29 (4.7)
Extracorporeal membrane oxygenation	6 (1.0)

All data are expressed as n (%).
* Non-exclusive criteria.

cohort of pregnant women with COVID-19, more than one fifth required respiratory support, with 15 % categorized with severe and 6% with critical disease. Although these rates may be overestimated because the study took place mainly in tertiary referral centers and included mostly symptomatic women, maternal respiratory morbidity related to COVID-19 appears notably higher than previously reported among symptomatic pregnant women [2,3]. A more precise estimate of the prevalence of the pulmonary complications would be provided by population-based studies; however, even those studies will not provide a "true" estimate because far from all pregnant women have been tested for SARS-CoV-2 in France during this period. Indeed, a recent UK population-based study of women hospitalized for COVID 19 reported 10 % (44/427) of the women needed critical care [6].

Our study shows that women with the most serious disease are those with the highest rates of comorbidities. Some, like obesity, diabetes, hypertension, or advanced age, have already been identified in general Chinese and US populations and among pregnant women in the UK [6,9–11]. In this cohort, however, gestational hypertensive diseases were also associated with severity. Risk factors for preeclampsia match those for COVID-19 severity [12]. The use of aggregated data makes it impossible to show an independent association between preeclampsia and COVID-19 severity. However, placental angiotensin-converting enzyme 2 (ACE2) is highly expressed at the maternal-fetal interface and its dysregulation by SARS-CoV-2 might be involved in the high rates of preeclampsia associated with severe and critical COVID-19 [13,14].

We also showed higher rates of preterm delivery than the Chinese studies [3,4]. In the UK study that included only hospitalized women, the rate of preterm birth before 37 weeks was 28 % among the 58 % of women whose pregnancy was completed by the end of follow-up [6]. In our series, because the women with the most severe illness are likely those who have already delivered, the rates of preterm births we report might be lower once all these women with COVID-19 during pregnancy have given birth. However, because more than 80 % of the women with critical COVID-19 have already delivered, the preterm delivery rates before 37 and 32 weeks in this group will not drop below 65 % and 40 %, respectively, even if all the other women of the group give birth after 36 weeks gestation.

Finally, two weeks after the imposition of lockdown, the number of pregnant women with active COVID-19 cases and with respiratory failure requiring invasive mechanical ventilation or ECMO decreased. Lockdown in France has been associated with a reduction of the estimated reproduction number from 3.3 to 0.5 [15], as also reported in China [16]. Because no treatment has yet been shown to be effective against SARS-CoV-2 infection [17], the temporal association between lockdown and the decrease in critical COVID-19 cases suggests that prevention measures such as lockdown could represent the only available policy for reducing the incidence of COVID-19 respiratory complications, especially among pregnant women with comorbidities.

This preliminary report has several limitations. All the data come from a research hospital network, of which more than two third are referral centers. Consequently, the morbidity observed is not an accurate estimate of the severity of COVID-19 in pregnant women because some cases were followed in other centers and referred because they already required oxygen therapy or were in critical condition. Regarding the risk factors of severity, because we used aggregated and not individual data, we were unable to

Table 2
Maternal characteristics and maternal, pregnancy and neonatal outcomes according to COVID-19 severity among pregnant women in France.

Outcomes	All N = 617	Non-severe N = 489	Requiring oxygen N = 93	Critical N = 35	*P* for trends	Any respiratory support N = 128	RR 95 % CI*
Maternal characteristics							
Age > 35	194 (31.4)	135 (27.6)	41 (44.1)	18 (51.4)	<0.001	59 (46.1)	1.7 (1.3–2.1)
Body mass index before pregnancy > 30	139 (22.5)	93 (19.0)	29 (31.2)	17 (48.6)	<0.001	46 (36.0)	1.9 (1.4–2.5)
Asthma	37 (6.0)	28 (5.7)	6 (6.5)	3 (8.6)	0.50	9 (7.0)	1.2 (0.6–2.5)
Other chronic respiratory disease	6 (1.0)	4 (0.8)	1 (1.1)	1 (2.9)	0.30	2 (1.6)	1.9 (0.4–10.3)
Preexisting diabetes type 1 or 2	14 (2.3)	7 (1.4)	6 (6.5)	1 (2.9)	0.04	7 (5.5)	3.8 (1.4–10.7)
History of preeclampsia	27 (4.4)	15 (3.1)	8 (8.6)	4 (11.4)	0.001	12 (9.4)	3.1 (1.5–6.4)
Chronic hypertension	18 (2.9)	11 (2.2)	4 (4.3)	3 (8.6)	0.02	7 (5.5)	2.4 (0.96–6.1)
Gestational diabetes	71 (11.5)	54 (11.0)	14 (15.1)	3 (8.6)	0.78	17 (13.3)	1.2 (0.7–2.0)
Gestational hypertension or preeclampsia	21 (3.4)	13 (2.7)	4 (4.3)	4 (11.4)	0.01	8 (6.2)	2.4 (1.0–5.6)
Smoking during pregnancy	16 (2.6)	11 (2.2)	5 (5.4)	0	–	5 (3.9)	1.7 (0.6–4.9)
Maternal outcomes**							
Maternal death	1 (0.2)	0	0	1 (2.9)	–	1 (0.8)	–
Recovered from COVID-19	486 (78.8)	391 (80.0)	75 (80.6)	20 (57.1)	0.05	95 (74.2)	–
Delivered	181 (29.3)	123 (25.1)	29 (31.2)	29 (82.9)	<0.001	58 (45.3)	–
Cesarean	87/181 (48.1)	39/123 (31.7)	25/29 (86.2)	23/29 (79.3)	<0.001	48/58 (82.8)	–
Cesarean for COVID-19 symptoms	45/181 (24.9)	4/123 (3.3)	19/29 (65.5)	22/29 (75.9)	<0.001	41/58 (70.7)	–
Pregnancy outcomes**							
Fetal loss at 14–21 wk	5/181 (2.8)	5/123 (4.1)	0	0	–	0	–
Preterm birth at 22–31 wk	21/181 (11.6)	3/123 (2.4)	4/29 (13.8)	14/29 (48.3)	<0.001	18/58 (31.0)	–
Preterm birth at 32–36 wk	29/181 (16.0)	10/123 (8.1)	10/29 (34.5)	9/29 (31.0)	<0.001	19/58 (32.8)	–
Overall preterm birth at 22–36 wk	50/181 (27.6)	13/123 (10.6)	14/29 (48.3)	23/29 (79.3)	<0.001	37/58 (63.8)	–
Intrauterine or intrapartum fetal death	7/181 (1.3)	5/123 (1.0)	0/29	2/29 (6.9)	–	2/58 (3.4)	–
Neonatal outcomes,***							
SARS-CoV-2 positive	2/190 (1.1)	1 (0.8)	1 (3.4)	0	–		–
Admission in Neonatal Intensive Care Unit	37/190 (19.5)	10/131 (7.6)	14/30 (46.7)	13/29 (44.8)	<0.001	27/59 (45.8)	–
Neonatal death	1/190 (0.5)	0	0	1 (3.4)	–	1/59 (1.7)	–

All data are expressed as n (%).
There were no missing values for maternal characteristics, previous medical history, or outcomes. Gestational diabetes was considered to be present if diagnosed and positive and otherwise was assumed to be negative. Smoking during pregnancy was assumed to be negative if it not reported.
* non-severe compared with any respiratory support (oxygen-requiring + critical).
** As only 181 of 617 women had given birth by April 14, 2020, RRs were not calculated for maternal, pregnancy and neonatal outcomes.
*** Eight multiple pregnancies (one triplet).

perform adjustments with multivariate models to establish the independence of these associations; other studies, preferably population-based, are necessary to confirm these findings.

In conclusion, COVID-19 in French pregnant women can be a serious condition and may be responsible for severe acute, potentially deadly respiratory distress syndromes. The most vulnerable pregnant women, those with comorbidities, may particularly benefit from prevention measures such as a lockdown.

Author contributions

Concept and design: EA, FB, DG, CG, GK, OM, LS, TS
Acquisition, analysis, or interpretation of data: All coauthors
Drafting of the manuscript: GK, TS
Critical revision of the manuscript for important intellectual content: EA, CG, GK, PR, LS, TS
Coordination and statistical analysis: GK
Administrative, technical, or material support: CG
Supervision: GK, TS

Declaration of Competing Interest

Dr Sentilhes reported consultancy work for Ferring laboratories. No other disclosures were reported.

Acknowledgment

Jo Ann Cahn for editing the manuscript.

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