Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Article

Impact of COVID-19 infection in pregnancy and neonates: A case control study.

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ICU, intensive care unit
NICU, neonatal intensive care unit
SD, standard deviation
WG, weeks of gestation

ABSTRACT

Objective: To evaluate maternal and neonatal outcomes of pregnant women who were infected by COVID-19 during pregnancy.
Study design: A Case control retrospective study was conducted in an Obstetrical Department of a west Parisian area during the first year of COVID-19 pandemic. Maternal and neonatal outcomes were compared between a group of women infected by the SARS-CoV-2 virus during pregnancy (March 2020- February 2021) and a control group of women delivering before pandemic. They were matched according to age and parity. Subgroups of SARS-CoV-2 infection occurring before vs after 37 weeks of gestations and symptomatic vs asymptomatic patients were analyzed. The rate of preterm birth, preeclampsia, placental abruption and stillbirth were compared between the year of pandemic and the year before for all deliveries.
Results: Maternal and neonatal outcomes were similar. Among the 86 pregnant women with SARS-CoV-2 infection, five were admitted to Hospital (5.8%). One was transferred in intensive care unit for respiratory distress (1.2%). All patients had favorable outcomes. Patients with symptoms had more associated comorbidities (34.5%, n = 20/58, with symptoms, vs 9,1%, n = 2/22, without symptoms, p = 0.023). No differences in preeclampsia, placenta abruption and stillbirth, but less preterm births (4.9%, n = 160/3383 vs 6.2%, n = 209/3235, p = 0.04) were observed between the year of pandemic and the year before.
Conclusion: There were few complications associated with COVID-19 infection among pregnant patients and their neonates. A low rate of associated comorbidities, a good access to healthcare services in this area and the small sample size of patients could explain these results.

Introduction

COVID-19 disease, caused by the SARS-CoV-2 virus, is a major public health problem. Since its appearance in 2019, the epidemic has spread quickly around the world. To date, more than five million deaths have been deplored, with a rate of 1.97% of deaths among positive cases [1]. Several studies have shown high rates of morbidity and mortality in populations with associated comorbidities including older age, obesity, type 2 diabetes, high blood pressure and immunosuppression [2]. Pregnant women have been described as an at-risk population, particularly during the third trimester because of decreased respiratory capacity and the weakness of the immune system [3]. In a recent metanalysis, the rate of pneumonia among hospitalized pregnant women infected by COVID-19 was 89% and the rate of admission in intensive care unit (ICU) was 8% [4]. Furthermore, COVID-19 infection may affect the course of a pregnancy with maternal and fetal complications. Pregnancies complications have been described (miscarriage, preeclampsia, intrauterine growth retardation, stillbirths), as well as complication during delivery (preterm labor and birth, increased risk of cesarian section), and in the postpartum period (postpartum hemorrhage) [5,6].

Some of these events could be related to the increased thrombotic risk during pregnancy and in COVID-19 infection. Indeed, some studies showed placenta micro thrombosis and maternofetal vascular malperfusion in patients infected with COVID-19 virus, even if asymptomatic [7]. As the COVID-19 infection remains a new pathology, there is a lack of data about outcomes in women that were infected in first and second trimester of pregnancy and in asymptomatic women.

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In this case control study, we evaluated the maternal and neonatal outcomes of pregnancies that were complicated with COVID-19 infection.

Material and methods

We designed a retrospective case control study including pregnant women who were infected by COVID-19 and followed up in the Obstetrical Department of Foch Hospital, located in the West Parisian area. This department consists in a type IIb maternity ward, which manages pregnancies from 31 weeks of gestation (WG). Near to 3500 births are registered every year in the maternity. An intensive care unit (ICU) for adults is also available on site. We included all pregnant patients diagnosed positive for the viral infection between March 2020 and February 2021. Patients were considered positive for the Sars-CoV-2 if the RT-PCR was positive. We systematically performed the test first for symptomatic cases and starting in September 2020, for all patients in labor and every hospitalized woman[8]. During this period, the original virus strain and Alpha variant (B.1.1.7) were mainly found.

We took as control group, pregnant women who delivered successively in September 2019, when COVID-19 disease had not yet appeared in France. A total of 286 patients were included in the study. We identified 86 patients with COVID-19 infection during pregnancy and 150 patients who delivered in September 2019. There was only singleton pregnancies in the group COVID-19, so we excluded 4 twin pregnancies in the control group. We matched cases and control based on age and parity. Matching was made according to propensity score (following a logistic regression) to limit selection bias. The pairs of patients were made with closest propensity score (difference < 0.1 point). We used an algorithm developed in SAS and named « Propensity Score Matching Macro » |9]. We finally obtained two groups of 86 patients. The flowchart of the study is available on Fig. 1.

Medical records were reviewed using the hospital's computerized database. Concerning mothers, the variables included: age, BMI before pregnancy, co-morbidities (defined as obesity, asthma, diabetes and high blood pressure), smoking, medical and obstetrical past history, maternal and fetal complications, RT-PCR positive test for COVID-19 virus, infection's term of pregnancy, presence of COVID-19 symptoms, biological analysis, treatments, hospitalization, transfer in ICU, delivery complications, postpartum outcomes and maternal death. Concerning newborn, the variables were: weight, Apgar score, pH and lactates at birth, presence of respiratory distress, infection or malformation, transfer to NICU and neonatal death.

A complementary analysis was made in order to evaluate rare complications, and thus reduce the biases due to undiagnosed and/or asymptomatic cases. We compared the proportion of preterm delivery, preeclampsia, stillbirths and placental abruption between the first year of pandemic (March 2020 and February 2021) and the year before (March 2019 and February 2020) among all patients who delivered in the Obstetric Department of Foch hospital during these two periods.

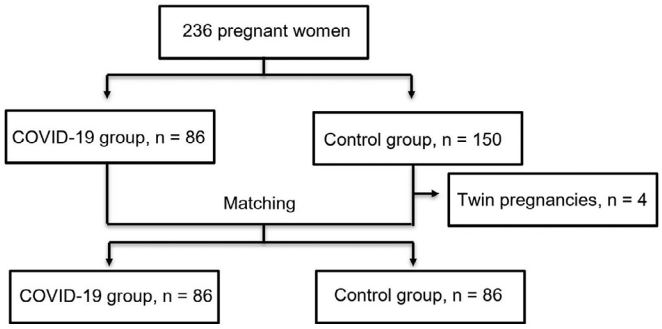

Fig. 1. Flowchart.

Statistical analysis was performed using descriptive evaluation with the mean (Standard deviation) for continuous variables and percentage for categorical variables. Fisher's exact test Wilcoxon, Student or Chi-square test were used to compare distribution ratios with a statistical significance set for a p value < 0.05. Microsoft Excel software was used for data recording and analyses were performed using SAS v9.4.

This study was approved by the hospital institutional review board (IRB00012437).

Results

We identified 86 patients infected by SARS-CoV-2 virus and 86 patients in the control group. Characteristics of patients are available in Table 1. Groups were similar according to BMI, associated comorbidities, ongoing infections, smoking, complications in previous pregnancies (gestational diabetes, preeclampsia, and postpartum hemorrhage).

In the COVID-19 group, there were 27.5% (n = 22) asymptomatic patients and 72.5% (n = 58) symptomatic ones. Symptoms relied to the viral infection are summarized in Fig. 2. Most common symptoms were fever (42.1%, n = 24) and cough (52,6%, n = 30). Only 5.8% (n = 5) of patients were admitted to the hospital because of associated fever and dyspnea. They were hospitalized for a period of one to twelve days. Rate of severe complications of COVID 19 defined by hospitalization in intensive care unit was 1.2% (n = 1).

One of the five patients admitted to hospital had the COVID-19 infection during the second trimester of pregnancy. She had a short hospitalization of one day and didn't need any specific treatment. Another patient had the infection at 37 WG, but did not receive any specific treatment. Her C-section originally scheduled at 39 WG (history of 2 C-sections) was advanced by 2 weeks because of COVID-19 infection. The last three patients received preventive dose of anticoagulants. One of them stayed in hospital for five days. She didn't need oxygen therapy, but received antenatal corticosteroid therapy for fetal lung maturation because she was at 30 WG. Another one stayed for three days in hospital. She had a thoracic computed tomography which showed typical lesions related to COVID-19 infection. She didn't need oxygen therapy. She didn't receive antenatal corticosteroids therapy for fetal lung maturation because she was at 34 WG. All had favorable outcomes and gave birth between 38 and 41 WG of heathy children. The last one was infected at 28 WG. She was 30 years old and didn't have any comorbidity, except being overweight with BMI at 28 kg/m^2. She had a respiratory distress and severe injuries on a thoracic computed tomography but no pulmonary embolism. She was transferred to an ICU in another hospital because of associated neonatal ICU available in case of premature delivery under 31 WG. She had prolonged corticosteroid treatment for fetal lung maturation and COVID-19 infection. She received magnesium sulfate treatment for fetal cerebral protection. In the ICU, she had oxygen therapy (45 L of oxygen with high flow oxygen system using Optiflow^{TM}) for six days. She developed a secondary pulmonary infection and received additional antibiotics. She stayed in the ICU for eight days and in hospital a total of twelve days. Her pregnancy was closely monitored with specialized ultrasound and a fetal MRI that revealed no anomaly. She later gave birth to a healthy and eutrophic child at 41 WG with a C-section due to lack of progression of the fetus. Delivery was complicated by post-partum hemorrhage of 500 mL with uterine atony, treated by sulprostone and Bakri balloon. She stayed one night in the ICU for monitoring.

Among pregnant women with COVID-19 infection who had blood test, we found biological disturbances: 29.2% (n = 7/24) had lymphopenia, 75.9% (n = 22/29) had an increase CRP, 75% (n = 12/16) had an increased LDH, and 100% (n = 11/11) had increased D-Dimers.

Table 1
Characteristics of patients.

			Control $N = 86$	COVID-19 $N = 86$	p
Age at birth		Mean (SD)	32.1 (5.0)	31.9 (4.6)	0.82
Parity post childbirth	Primiparity Multiparity	n (%)	44 (51.2%) 42 (48.8%)	47 (54.7%) 39 (45.3%)	0.65
Body mass index before pregnancy	≤ 30 kg/m^2	n (%)	59 (72.0%)	63 (78.8%)	0.32
	> 30 kg/m^2		23 (28.0%)	17 (21.3%)	
History of :					
Asthma		n (%)	4 (4.6%)	5 (5.8%)	0.74
High blood pressure		n (%)	0	0	
Diabetes		n (%)	0	1 (1.2%)	0.32
Gestational diabetes		n (%)	3 (3.5%)	1 (1.2%)	0.32
Preeclampsia		n (%)	0	1 (1.2%)	0.32
Postpartum hemorrhage		n (%)	3 (3.5%)	2 (2.3%)	0.66
Ongoing pregnancy:					
Other infection		n (%)	2 (2.3%)	0	0.50
Smoking		n (%)	9 (10.5%)	3 (3.5%)	0.08

Table 2 shows the course of pregnancies complicated with the viral infection. There were no more complications such as gestational diabetes, high blood pressure, threat of preterm birth, intrauterine growth retardation, fetal malformations and oligohydramnios in the COVID-19 group. There was no stillbirth, eclampsia, preeclampsia, placental abruption, HELLP syndrome, thrombosis in the two groups. There was one late miscarriage in COVID-19 group, away from the term of infection, without any etiology found.

Table 3 shows materno-fetal outcomes. The average birth term was not statistically different between the two groups (39.29± 2.65WGfor cases vs 39.49± 2.08WG for controls, $p = 0.555$). There were no statistically differences between two groups in proportions of spontaneous delivery, instrumental delivery and C-section. Three patients had a labor induction because of COVID-19 infection. There was no more postpartum hemorrhage in the COVID-19 group.

We haven't identified any difference regarding the newborn conditions. In COVID-19 group, there were no more neonatal respiratory distress (5.9%, $n = 5/86$, vs 3.5%, $n = 3/86$, $p = 0.72$), neonatal infection (0%, vs 1.2%, $n = 1/86$, $p = 1$), malformation (none in both groups) or transfer in NICU (5.9%, $n = 5/86$, vs 5.8%, $n = 5/86$, $p = 1$).

The subgroup analysis according to when the COVID-19 infection occurred (before or after 37 weeks of gestation) had no impact on the mode of delivery. There were more cases of induction of labor in the COVID-19 infection group if the infection occurred after 37 weeks of gestation than before (9.7%, $n = 3/31$, vs0%, 0/53, $p = 0.03$). There was no statistical difference in fetal complications (Table 3).

The subgroup analysis according to the presence or absence of symptoms showed no difference in birth term or in the mode of delivery. Patients with symptoms had more associated comorbidities than asymptomatic ones (34.5%, $n = 20/58$, vs 9.1%, $n = 2/22$, $p = 0.02$). There was more threat of preterm birth in asymptomatic patients (13.6%, $n = 3/22$ vs0/58, $p = 0.02$) (Table 2). If only symptomatic cases were compared to a control group, no difference in materno-foetal outcomes were observed (supplementary Table 1).

In Fig. 3, we compared the occurrence of four complications: we found no differences in the prevalence of stillbirth (0.4%, $n = 14/3235$, vs 0.3%, $n = 10/3383$, $p = 0.06$), placental abruption (0.1%, $n = 4/3235$, vs 0.2%, $n = 6/3383$, $p = 0.57$), preeclampsia (1.7%, $n = 58/3235$, vs 1.7%, $n = 56/3383$, $p = 0.67$) between the year before and the year of pandemic. However, our analyses found a significant decrease of preterm birth (6.2%, $n = 209/3235$, vs 4.9%, $n = 160/3383$, $p = 0.04$).

Discussion

This study involved pregnant women who were infected by SARS-CoV-2 virus during the first year of COVID-19 pandemic, (March 2020 -February 2021). It was conducted in an Obstetrical Department of a West Parisian area.

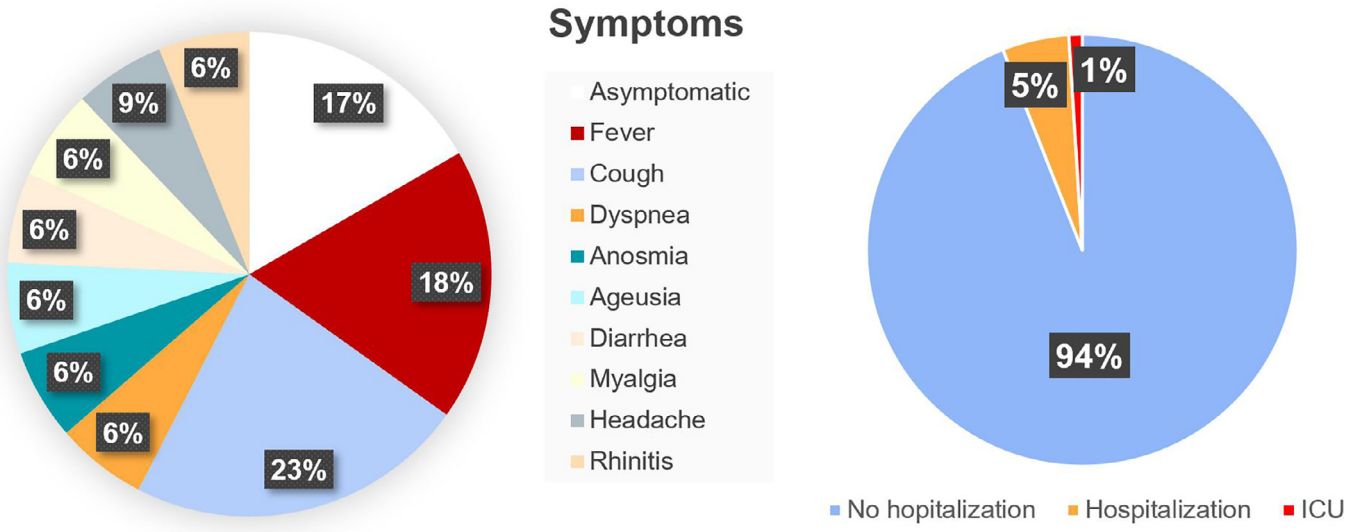

Fig. 2. Color pie chart showing clinical picture and hospitalization rate.

Table 2
Course of pregnancy.

		Control*N* = 86	COVID-19*N* = 86	p	PCR+ < 37 SA *N* = 53	PCR+ ≥ 37 SA *N* = 31	p	Symptoms *N* = 58	No symptoms *N* = 22	p
Comorbidities	n (%)	24 (27.9%)	22 (25.6%)	0.73	–	–	–	20 (34.5%)	2 (9.1%)	0.02*
Gestational diabetes	n (%)	14 (16.3%)	11 (12.8%)	0.52	6 (11.3%)	5 (16.1%)	0.52	8 (13.8%)	3 (13.6%)	1.00
High blood pressure	n (%)	0	0	–	0	0	–	0	0	–
Threat of preterm birth	n (%)	4 (4.7%)	3 (3.5%)	1.00	2 (3.8%)	1 (3.2%)	1.00	0	3 (13.6%)	0.02*
Intra uterine growth retardation	n (%)	6 (7.0%)	10 (11.8%)	0.28	6 (11.5%)	4 (12.9%)	1.00	7 (12.3%)	2 (9.1%)	1.00
Oligohydramnios	n (%)	6 (7.0%)	2 (2.4%)	0.28	1 (1.9%)	1 (3.2%)	1.00	1 (1.8%)	1 (4.5%)	0.48
Malformation	n (%)	0	0	–	0	0	–	0	0	–

Table 3
Materno-fetal outcomes.

		Control*N* = 86	COVID-19*N* = 86	p	PCR+ < 37 SA *N* = 53	PCR+ ≥ 37 SA *N* = 31	p	Symptoms *N* = 58	No symptoms *N* = 22	p
Birth gestationnal age	Mean (SD)	39.49 (2.08)	39.29 (2.65)	0.55	39.24 (3.23)	39.44 (1.35)	0.59	39.69 (1.23)	39.39 (1.29)	0.28
Spontaneous delivery	n (%)	53 (61.6%)	48 (56.5%)	0.49	27 (51.9%)	20 (64.5%)	0.26	33 (57.9%)	11 (50.0%)	0.53
Induced labor for COVID-19	n (%)	0	3 (3.5%)	0.08	0	3 (9.7%)	0.03*	2 (3.4%)	1 (4.5%)	0.82
C-section	n (%)	19 (22.1%)	22 (25.9%)	0.56	14 (26.9%)	7 (22.6%)	0.66	12 (21.1%)	8 (36.4%)	0.16
C-section for COVID-19	n (%)	0	1 (1,2%)	0.3	0	1 (3,2%)	0.19	1 (1,7%)	0	0.53
C-section for fetal heart rate	n (%)	2 (2.3%)	7 (8.1%)	0.10	5 (9.4%)	1 (3.2%)	0.32	3 (5.2%)	3 (13.6%)	0.24
Postpartum hemorrhage	n (%)	3 (3.5%)	4 (4.7%)	0.72	2 (3.8%)	2 (6.5%)	0.63	2 (3.5%)	2 (9.1%)	0.31
New born's weight (g)	Mean (SD)	3282.0 (447.5)	3362.6 (465.6)	0.25	3394.3 (405.9)	3306.5 (521.9)	0.43	3371.3 (436.3)	3376.8 (573.1)	0.97
Apgar 1 min	Mean (SD)	9.1 (1.8)	9.4 (1.6)	0.09	9.4 (1.9)	9.4 (1.3)	0.53	9.4 (1.5)	9.7 (0.8)	0.28
Apgar 5 min	Mean (SD)	9.8 (0.7)	9.8 (1.2)	0.74	9.7 (1.5)	9.9 (0.3)	0.59	9.9 (0.5)	10.0 (0.2)	0.50
pH	Mean (SD)	7.23 (0.10)	7.24 (0.09)	0.65	7.25 (0.09)	7.23 (0.09)	0.22	7.24 (0.09)	7.24 (0.10)	0.93
Lactate	Mean (SD)	4.53 (2.28)	4.09 (2.00)	0.25	4.11 (2.04)	4.04 (2.03)	0.81	4.05 (2.06)	4.20 (2.08)	0.70
New born's transfer in ICU	n (%)	5 (5.8%)	5 (5.9%)	1.000	2 (3.8%)	3 (9.7%)	0.357	3 (5.3%)	2 (9.1%)	0.614
New born's respiratory distress	n (%)	3 (3.5%)	5 (5.9%)	0.720	2 (3.8%)	3 (9.7%)	0.357	2 (3.5%)	3 (13.6%)	0.129
New born's infection	n (%)	1 (1.2%)	0	1.000	0	0	–	0	0	–

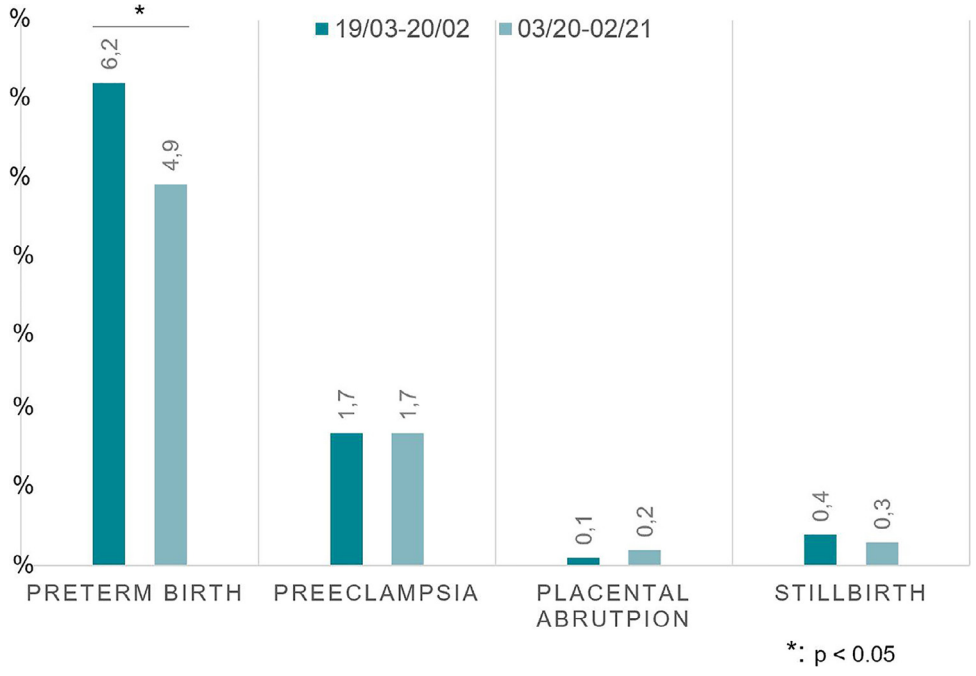

Fig. 3. Histogram of preeclampsia, placental abruption and intra uterine death between 2019 and 2020 period.

Among 86 patients infected by the virus, 5.8% needed hospitalization, 1.2% only were admitted in the ICU and there was no fatal outcome. We confirmed that pregnancy is an independent factor of severe forms [4,10]. However, our rate of hospitalization, especially in ICU was low: In literature this rate varies from 8 to 9.8% [4,10]. The risk of maternal mortality was 1.6% in a multinational cohort study [11], 22 times higher in the group of pregnant women with COVID-19 infection. These deaths were concentrated in institutions from less developed regions with thinly available ICU services. Our low rate of severe forms of COVID-19 infection and mortality could be explained by an appropriate health care service system, a high socioeconomic level in this area and few preexisting comorbidities, except for obesity. Indeed, our rate of obesity was higher than in general population [12]. Vivanti and al. showed that pregnant women suffering from obesity had higher risk to be admitted to ICU [13]. In a recent metanalysis, diabetes was the most common associated comorbidity, found in 18% of pregnant women with COVID-19 infection [6]. These comorbidities increase the risks of severity of the COVID-19 infection. The population of this study had a low rate of diabetes. According to Allotey et al., pregnant women had lower risk to develop symptoms than non-pregnant women, but had a higher risk of serious complications if they had associated comorbidities [14]. In our experience, COVID-19 patients were more likely symptomatic if they had associated comorbidities.

Five patients were hospitalized for fever and dyspnea. French guidelines recommend hospitalization and blood tests for pregnant women with oxygen-requiring pneumonia, or associated comorbidities [15]. Our laboratory findings are in line with literature: lymphopenia, increased values of C reactive protein and Dehydrogenase lactate were observed [6]. In case of dyspnea, a thoracic computed tomography should be realized to evaluate the expanse of lesions and associated pulmonary embolism. Antibiotics need to be added if bacterial superinfection is found [15]. Preventive dose anticoagulants are widely performed if medium or high thromboembolic risk were associated [16]. Corticoid treatment are used for fetal lung maturation and severe hypoxia [17]. ICU transfer is necessary in case of increased oxygen requirement therapy or arterial partial pressure of oxygen (PaO2) under 70 mmHg [15]. ICU Practices have evolved since the beginning of the pandemic. Intubation is now avoided if possible due to the later difficulty of weaning. cesarian sections were first widely performed in case of worsening respiratory status of patients. This led to increased preterm births performed under general anesthesia with intubation [6,18,19]. They are now avoided and the use of high flow nasal oxygen therapy (Optiflow) allows to go through the acute phase of the disease in most severe forms without premature birth and C -section [20]. Furthermore, the rate of C-sections varies a lot between different countries and health care service system [21]. We didn't have more C-section, prematurity, or induction of labor for COVID-19 infection in our study. There is controversial associations with postpartum hemorrhage in literature [22,23].

Surprisingly, the rate of maternal complications was not increased in the cohort of patients infected by the virus. Even if we compare the whole cases of preeclampsia, placental abruption and stillbirth between the year before and during the pandemic, we still don't have significant difference. When comparing to literature, It seems that there is heterogenous results about the effect of SARS-CoV-2 virus on materno-fetal outcomes: the clinical course of 1100 pregnancies wasn't significantly influenced by COVID-19 infection according to Di Toro and al. [4]. Association with low birth rate was found in some trials, but not in other ones [24]. While COVID-19 infection and pregnancy were shown to be associated with hypercoagulability, excess risk of veinous thrombosis is debatable in literature [16]. However, higher incidence of preeclampsia or "preeclampsia like" syndrome is clearly demonstrated and evaluated around 10.5–16.2% [18,19]. Fortunately, mortality remains a rare complication among pregnant women infected by COVID-19 and their fetuses [4,5,18,25]. De Sisto et al. report*ed* a higher incidence of stillbirth in patient infected with SARS-CoV-2 virus especially with Delta variant. In France, the Delta variant appeared after the end of our study, which may explain that the rate of stillbirth has remained stable [26]. The pandemic had also an effect not directly related to COVID-19 infection but related to change of lifestyle induced (lockdown, teleworking). In line with literature, we found a decrease of preterm birth during the pandemic probably due to the lockdowns [27].

Neonatal outcomes were not statistically different between the two groups. Transfers to NICU were made in 5.9% of newborns from patients in COVID-19 group. In literature, prevalence of transfer in NICU for neonates varied from 2 to 30% [4,5]. We didn't observed cases of vertical transmission. Vertical transmission occurred in a minority of cases and COVID-19 in neonates was mostly benign [4,6,18].

The subgroups analyses showed no more complication according to the term of occurrence of COVID-19 infection. Patients who developed infection after 37 WG were more likely to have induced labor for COVID-19 infection. Most of studies showed that pregnant women had higher risk to contract COVID-19 infection during the third trimester of pregnancy [25]. COVID-19 infection during first and second trimester didn't seem to be associated with serious complications [28]. In our study, asymptomatic patients had higher risk of threat of preterm birth. In literature, findings showed higher risk of complications amongst symptomatic patients and reassuring data in asymptomatic ones except for associated preeclampsia [11]. The proportion of asymptomatic patients within pregnancy seem to be higher than in general population [29].

One of the limits of our study is the possibility that some cases were not diagnosed. We have chosen to include only pregnant women with a COVID-19 infection confirmed by a positive PCR test. We have probably missed COVID-19 infections at the very beginning of the pandemic when PCR test were not available, as well as undiagnosed symptomatic and asymptomatic cases. However, complications have been described even after asymptomatic cases especially for preeclampsia [11]. Another bias is due to the small sample size of our population. Thus, rare complications could have been missed. To try to evaluate the rate of rare complications, we Compared two study periods (March 2019 to February 2020 and March 2020 to February 2021) concerning preeclampsia, stillbirth, placental abruption and premature delivery among all the patients who delivered in our unit. Unfortunately, other parameters have been modified between these two periods (successive lockdowns and development of teleconsultations for example) and may have had an impact on the results. The inclusion of patients in 2019 in the control group exposes to bias. Ideally, our control group should have been chosen in the same period with patients who didn't were positive to SARS-CoV-2 during pregnancy. This was unfortunately impossible as regular testing during pregnancy and serology weren't systematically performed at the end of the pregnancy in our population. Our prevalence rate of COVID-19 infection was probably underestimated (2.6%). In another Parisian Hospital, Tsatsaris et al. had a prevalence rate of 4.7% during first months of the pandemia [30]. Finally, all retrospective evaluations add bias and lost-of follow up patients can't be excluded.

Conclusion

The findings of this study are reassuring. We had few severe cases, maternal et fetal complications in pregnant women infected by SARS-CoV-2 virus. COVID-19 infection appears to be an independent risk factor for adverse outcomes but fortunately they remain rare. This study allows to enrich the clinical data concerning the COVID-19 infection and pregnancy especially focused on the first year of the pandemic in a Parisian area with privileged access to care and a good socioeconomic level. As COVID-19 is still a new disease, a better understanding of the mechanism and the course of infection are needed especially about thrombotic effect, placental modifications,

and immunological changes in pregnancy. Furthermore, the arrival of new variants may change the game.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jogoh.2022.102366.

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