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

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ABBREVIATIONS

BMI: Body mass index

ICU: intensive care unit

NICU: neonatal intensive care unit

SD: standard deviation

WG: weeks of gestation

1 ABSTRACT

2 Objective: To evaluate maternal and neonatal outcomes of pregnant women who were
3 infected by COVID-19 during pregnancy.

4 Study design: A Case control retrospective study was conducted in an Obstetrical
5 Department of a west Parisian area during the first year of COVID-19 pandemic. Maternal
6 and neonatal outcomes were compared between a group of women infected by the SARS-
7 CoV-2 virus during pregnancy (March 2020- February 2021) and a control group of women
8 delivering before pandemic. They were matched according to age and parity. Subgroups of
9 SARS-CoV-2 infection occurring before vs after 37 weeks of gestations and symptomatic vs
10 asymptomatic patients were analyzed. The rate of preterm birth, preeclampsia, placental
11 abruption and stillbirth were compared between the year of pandemic and the year before
12 for all deliveries.

13 Results: Maternal and neonatal outcomes were similar. Among the 86 pregnant women with
14 SARS-CoV-2 infection, five were admitted to Hospital (5.8%). One was transferred in
15 intensive care unit for respiratory distress (1.2%). All patients had favorable outcomes.
16 Patients with symptoms had more associated comorbidities (34.5%, n=20/58, with
17 symptoms, vs 9,1%, n=2/22, without symptoms, p=0.023). No differences in preeclampsia,
18 placenta abruption and stillbirth, but less preterm births (4.9 %, n=160/3383 vs 6.2 %,
19 n=209/3235, p=0.04) were observed between the year of pandemic and the year before.

20 Conclusion: There were few complications associated with COVID-19 infection among
21 pregnant patients and their neonates. A low rate of associated comorbidities, a good access
22 to healthcare services in this area and the small sample size of patients could explain these
23 results.

24

25 KEYWORDS

26 COVID-19, infection, Pregnancy, neonatal outcomes, complications.

27 INTRODUCTION

28 COVID-19 disease, caused by the SARS-CoV-2 virus, is a major public health problem. Since
29 its appearance in 2019, the epidemic has spread quickly around the world. To date, more
30 than five million deaths have been deplored, with a rate of 1.97% of deaths among positive
31 cases [1]. Several studies have shown high rates of morbidity and mortality in populations
32 with associated comorbidities including older age, obesity, type 2 diabetes, high blood
33 pressure and immunosuppression [2]. Pregnant women have been described as an at-risk
34 population, particularly during the third trimester because of decreased respiratory capacity
35 and the weakness of the immune system [3]. In a recent metanalysis, the rate of pneumonia
36 among hospitalized pregnant women infected by COVID-19 was 89% and the rate of
37 admission in intensive care unit (ICU) was 8% [4]. Furthermore, COVID-19 infection may
38 affect the course of a pregnancy with maternal and fetal complications. Pregnancies
39 complications have been described (miscarriage, preeclampsia, intrauterine growth
40 retardation, stillbirths), as well as complication during delivery (preterm labor and birth,
41 increased risk of cesarian section), and in the postpartum period (postpartum hemorrhage)
42 [5,6].

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

47 about outcomes in women that were infected in first and second trimester of pregnancy and
48 in asymptomatic women.

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

51

52 MATERIAL AND METHODS

53 We designed a retrospective case control study including pregnant women who were
54 infected by COVID-19 and followed up in the Obstetrical Department of Foch Hospital,
55 located in the West Parisian area. This department consists in a type IIb maternity ward,
56 which manages pregnancies from 31 weeks of gestation (WG). Near to 3,500 births are
57 registered every year in the maternity. An intensive care unit (ICU) for adults is also available
58 on site. We included all pregnant patients diagnosed positive for the viral infection between
59 March 2020 and February 2021. Patients were considered positive for the Sars-CoV-2 if the
60 RT-PCR was positive. We systematically performed the test first for symptomatic cases and
61 starting in September 2020, for all patients in labor and every hospitalized woman. During
62 this period, the original virus strain and Alpha variant (B.1.1.7) were mainly found.

63 We took as control group, pregnant women who delivered successively in September 2019,
64 when COVID-19 disease had not yet appeared in France. A total of 286 patients were
65 included in the study. We identified 86 patients with COVID-19 infection during pregnancy
66 and 150 patients who delivered in September 2019. There was only singleton pregnancies in
67 the group COVID-19, so we excluded 4 twin pregnancies in the control group. We matched
68 cases and control based on age and parity. Matching was made according to propensity
69 score (following a logistic regression) to limit selection bias. The pairs of patients were made

70 with closest propensity score (difference < 0.1 point). We used an algorithm developed in
71 SAS and named « Propensity Score Matching Macro » [9]. We finally obtained two groups of
72 86 patients. The flow chart of the study is available on Figure 1.

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

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

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

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

94

95 RESULTS

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

100 In the COVID-19 group, there were 27.5% (n=22) asymptomatic patients and 72.5% (n=58)
101 symptomatic ones. Symptoms related to the viral infection are summarized in Figure 2. Most
102 common symptoms were fever (42.1%, n=24) and cough (52.6%, n=30). Only 5.8 % (n=5) of
103 patients were admitted to the hospital because of associated fever and dyspnea. They were
104 hospitalized for a period of one to twelve days. Rate of severe complications of COVID 19
105 defined by hospitalization in intensive care unit was 1.2% (n=1).

106 One of the five patients admitted to hospital had the COVID-19 infection during the second
107 trimester of pregnancy. She had a short hospitalization of one day and didn't need any
108 specific treatment. Another patient had the infection at 37 WG, but did not receive any
109 specific treatment. Her C-section originally scheduled at 39 WG (history of 2 C-sections) was
110 advanced by 2 weeks because of COVID-19 infection. The last three patients received
111 preventive dose of anticoagulants. One of them stayed in hospital for five days. She didn't
112 need oxygen therapy, but received antenatal corticosteroid therapy for fetal lung maturation
113 because she was at 30 WG. Another one stayed for three days in hospital. She had a thoracic
114 computed tomography which showed typical lesions related to COVID-19 infection. She
115 didn't need oxygen therapy. She didn't receive antenatal corticosteroids therapy for fetal
116 lung maturation because she was at 34 WG. All had favorable outcomes and gave birth
117 between 38 and 41 WG of healthy children. The last one was infected at 28 WG. She was 30

118 years old and didn't have any comorbidity, except being overweight with BMI at 28 kg/m².
119 She had a respiratory distress and severe injuries on a thoracic computed tomography but
120 no pulmonary embolism. She was transferred to an ICU in another hospital because of
121 associated neonatal ICU available in case of premature delivery under 31 WG. She had
122 prolonged corticosteroid treatment for fetal lung maturation and COVID-19 infection. She
123 received magnesium sulfate treatment for fetal cerebral protection. In the ICU, she had
124 oxygen therapy (45 L of oxygen with high flow oxygen system using Optiflow™) for six days.
125 She developed a secondary pulmonary infection and received additional antibiotics. She
126 stayed in the ICU for eight days and in hospital a total of twelve days. Her pregnancy was
127 closely monitored with specialized ultrasound and a fetal MRI that revealed no anomaly. She
128 later gave birth to a healthy and eutrophic child at 41 WG with a C-section due to lack of
129 progression of the fetus. Delivery was complicated by post-partum hemorrhage of 500 mL
130 with uterine atony, treated by sulprostone and Bakri balloon. She stayed one night in the ICU
131 for monitoring.

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

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

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

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

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

155 The subgroup analysis according to the presence or absence of symptoms showed no
156 difference in birth term or in the mode of delivery. Patients with symptoms had more
157 associated comorbidities than asymptomatic ones (34.5%, $n=20/58$, vs 9.1%, $n=2/22$,
158 $p=0.02$). There was more threat of preterm birth in asymptomatic patients (13.6%, $n=3/22$
159 vs $n=0/58$, $p=0.02$) (Table 2). If only symptomatic cases were compared to a control group, no
160 difference in materno-foetal outcomes were observed (supplementary table 1).

161 In Figure 3, we compared the occurrence of four complications: we found no differences in
162 the prevalence of stillbirth (0.4%, $n=14/3235$, vs 0.3%, $n=10/3383$, $p=0.06$), placental
163 abruption (0.1%, $n=4/3235$, vs 0.2%, $n=6/3383$, $p=0.57$), preeclampsia (1.7%, $n=58/3235$, vs

164 1.7%, n=56/3383, p=0.67) between the year before and the year of pandemic. However, our
165 analyses found a significant decrease of preterm birth (6.2 %, n=209/3235, vs 4.9 %, n=160/3383, p=0.04).

167

168 **DISCUSSION**

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

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

187 than non-pregnant women, but had a higher risk of serious complications if they had
188 associated comorbidities [14]. In our experience, COVID-19 patients were more likely
189 symptomatic if they had associated comorbidities.

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

210 Surprisingly, the rate of maternal complications was not increased in the cohort of patients
211 infected by the virus. Even if we compare the whole cases of pre-eclampsia, placental
212 abruption and stillbirth between the year before and during the pandemic, we still don't
213 have significant difference. When comparing to literature, It seems that there is
214 heterogenous results about the effect of SARS-CoV-2 virus on materno-fetal outcomes: the
215 clinical course of 1100 pregnancies wasn't significantly influenced by COVID-19 infection
216 according to Di Toro and al. [4]. Association with low birth rate was found in some trials, but
217 not in other ones [24]. While COVID-19 infection and pregnancy were shown to be
218 associated with hypercoagulability, excess risk of veinous thrombosis is debatable in
219 literature [16]. However, higher incidence of preeclampsia or "preeclampsia like" syndrome
220 is clearly demonstrated and evaluated around 10.5-16.2% [18,19]. Fortunately, mortality
221 remains a rare complication among pregnant women infected by COVID-19 and their fetuses
222 [4,5,18,25]. De Sisto et al. reported a higher incidence of stillbirth in patient infected with
223 SARS-CoV-2 virus especially with Delta variant. In France, the Delta variant appeared after
224 the end of our study, which may explain that the rate of stillbirth has remained stable [26].
225 The pandemic had also an effect not directly related to COVID-19 infection but related to
226 change of lifestyle induced (lockdown, teleworking). In line with literature, we found a
227 decrease of preterm birth during the pandemic probably due to the lockdowns [27].

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

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

243 One of the limits of our study is the possibility that some cases were not diagnosed. We have
244 chosen to include only pregnant women with a COVID-19 infection confirmed by a positive
245 PCR test. We have probably missed COVID-19 infections at the very beginning of the
246 pandemic when PCR test were not available, as well as undiagnosed symptomatic and
247 asymptomatic cases. However, complications have been described even after asymptomatic
248 cases especially for preeclampsia [11]. Another bias is due to the small sample size of our
249 population. Thus, rare complications could have been missed. To try to evaluate the rate of
250 rare complications, we Compared two study periods (March 2019 to February 2020 and
251 March 2020 to February 2021) concerning preeclampsia, stillbirth, placental abruption and
252 premature delivery among all the patients who delivered in our unit. Unfortunately, other
253 parameters have been modified between these two periods (successive lockdowns and
254 development of teleconsultations for example) and may have had an impact on the results.
255 The inclusion of patients in 2019 in the control group exposes to bias. Ideally, our control
256 group should have been chosen in the same period with patients who didn't were positive to

257 SARS-CoV-2 during pregnancy. This was unfortunately impossible as regular testing during
258 pregnancy and serology weren't systematically performed at the end of the pregnancy in our
259 population. Our prevalence rate of COVID-19 infection was probably underestimated (2.6%).
260 In another Parisian Hospital, Tsatsaris et al. had a prevalence rate of 4.7% during first
261 months of the pandemic [30]. Finally, all retrospective evaluations add bias and lost-of
262 follow up patients can't be excluded.

263

264 CONCLUSION

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

274

275 **Declaration of Competing Interest**

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

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286 REFERENCES

- 287 1. WHO Coronavirus (COVID-19) Dashboard [Internet]. [cité 16 déc 2021]. Disponible sur:
288 <https://covid19.who.int>
- 289 2. Zhou Y, Chi J, Lv W, Wang Y. Obesity and diabetes as high-risk factors for severe coronavirus
290 disease 2019 (Covid-19). *Diabetes Metab Res Rev.* févr 2021;37(2):e3377.
- 291 3. Wastnedge EAN, Reynolds RM, van Boeckel SR, Stock SJ, Denison FC, Maybin JA, et al. Pregnancy
292 and COVID-19. *Physiol Rev.* 1 janv 2021;101(1):303-18.
- 293 4. Di Toro F, Gjoka M, Di Lorenzo G, De Santo D, De Seta F, Maso G, et al. Impact of COVID-19 on
294 maternal and neonatal outcomes: a systematic review and meta-analysis. *Clin Microbiol Infect.*
295 janv 2021;27(1):36-46.
- 296 5. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19)
297 on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol.*
298 juill 2020;56(1):15-27.
- 299 6. Jafari M, Pormohammad A, Sheikh Neshin SA, Ghorbani S, Bose D, Alimohammadi S, et al.
300 Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with
301 control patients: A systematic review and meta-analysis. *Rev Med Virol.* sept 2021;31(5):1-16.
- 302 7. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental Pathology in COVID-19.
303 *American Journal of Clinical Pathology.* 8 juin 2020;154(1):23-32.
- 304 8. Murtada R, Carbonnel M, Revaux A, Favre-Inhofer A, Ayoubi J-M. Managing a Department of
305 Obstetrics and Gynecology in Times of COVID-19 Outbreak: The Foch Hospital Experience. *Front*
306 *Surg.* 2021;8:564145.
- 307 9. Hardis Fraeman K., Application development of North-East SAS users group, Baltimore USA, Nov
308 2010.
- 309 10. Blitz MJ, Grünebaum A, Tekbali A, Bornstein E, Rochelson B, Nimaroff M, et al. Intensive care unit
310 admissions for pregnant and nonpregnant women with coronavirus disease 2019. *Am J Obstet*
311 *Gynecol.* août 2020;223(2):290-1.
- 312 11. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal
313 Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The
314 INTERCOVID Multinational Cohort Study. *JAMA Pediatr.* 1 août 2021;175(8):817-26.
- 315 12. Czernichow S, Renuy A, Rives-Lange C, Carette C, Airagnes G, Wiernik E, et al. Evolution of the
316 prevalence of obesity in the adult population in France, 2013-2016: the Constances study. *Sci*
317 *Rep.* 8 juill 2021;11(1):14152.
- 318 13. Vivanti AJ, Mattern J, Vauloup-Fellous C, Jani J, Rigonnot L, Hachem LE, et al. Retrospective
319 Description of Pregnant Women Infected with Severe Acute Respiratory Syndrome Coronavirus
320 2, France - Volume 26, Number 9—September 2020 - *Emerging Infectious Diseases journal - CDC.*
321 [cité 22 déc 2021]; Disponible sur: https://wwwnc.cdc.gov/eid/article/26/9/20-2144_article
- 322 14. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk
323 factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living
324 systematic review and meta-analysis. *BMJ.* 1 sept 2020;370:m3320.

- 325 15. Peyronnet V, Sibiude J, Huissoud C, Lescure F-X, Lucet J-C, Mandelbrot L, et al. [Infection with
326 SARS-CoV-2 in pregnancy. Update of Information and proposed care. CNGOF]. *Gynecol Obstet*
327 *Fertil Senol.* déc 2020;48(12):858-70.
- 328 16. Benhamou D, Keita H, Ducloy-Bouthors AS, Benhamou D, Bonnet MP, Bonnin M, et al.
329 Coagulation changes and thromboembolic risk in COVID-19 obstetric patients. *Anaesthesia*
330 *Critical Care & Pain Medicine.* 1 juin 2020;39(3):351-3.
- 331 17. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC,
332 Murthy S, Diaz JV, Slutsky AS, Villar J, et al. Association Between Administration of Systemic
333 Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis.
334 *JAMA.* 6 oct 2020;324(13):1330-41.
- 335 18. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus
336 spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-
337 analysis. *Am J Obstet Gynecol MFM.* mai 2020;2(2):100107.
- 338 19. Antoun L, Taweel NE, Ahmed I, Patni S, Honest H. Maternal COVID-19 infection, clinical
339 characteristics, pregnancy, and neonatal outcome: A prospective cohort study. *European Journal*
340 *of Obstetrics & Gynecology and Reproductive Biology.* 1 sept 2020;252:559-62.
- 341 20. Sykes DL, Crooks MG, Thu KT, Brown OI, Tyrer TJP, Rennardson J, et al. Outcomes and
342 characteristics of COVID-19 patients treated with continuous positive airway pressure/high-flow
343 nasal oxygen outside the intensive care setting. *ERJ Open Research [Internet].* 1 oct 2021 [cité 30
344 déc 2021];7(4). Disponible sur: <https://openres.ersjournals.com/content/7/4/00318-2021>
- 345 21. Dubey P, Reddy SY, Manuel S, Dwivedi AK. Maternal and neonatal characteristics and outcomes
346 among COVID-19 infected women: An updated systematic review and meta-analysis. *Eur J*
347 *Obstet Gynecol Reprod Biol.* sept 2020;252:490-501.
- 348 22. Wang MJ, Schapero M, Iverson R, Yarrington CD. Obstetric Hemorrhage Risk Associated with
349 Novel COVID-19 Diagnosis from a Single-Institution Cohort in the United States. *Am J Perinatol.*
350 *déc 2020;37(14):1411-6.*
- 351 23. Badr DA, Picone O, Bevilacqua E, Carlin A, Meli F, Sibiude J, et al. Severe Acute Respiratory
352 Syndrome Coronavirus 2 and Pregnancy Outcomes According to Gestational Age at Time of
353 Infection. *Emerg Infect Dis.* oct 2021;27(10):2535-43.
- 354 24. Melo GC de, Araújo KCGM de. COVID-19 infection in pregnant women, preterm delivery, birth
355 weight, and vertical transmission: a systematic review and meta-analysis. *Cad Saude Publica.*
356 *2020;36(7):e00087320.*
- 357 25. Karimi L, Makvandi S, Vahedian-Azimi A, Sathyapalan T, Sahebkar A. Effect of COVID-19 on
358 Mortality of Pregnant and Postpartum Women: A Systematic Review and Meta-Analysis. *J*
359 *Pregnancy.* 2021;2021:8870129.
- 360 26. DeSisto CL, Wallace B, Simeone RM, Polen K, Ko JY, Meaney-Delman D, et al. Risk for Stillbirth
361 Among Women With and Without COVID-19 at Delivery Hospitalization - United States, March
362 2020-September 2021. *MMWR Morb Mortal Wkly Rep.* 26 nov 2021;70(47):1640-5.
- 363 27. Graff I, De Broucker C, Vargas J, Vanoost A, Gondry J, Foulon A. [COVID-19 and lockdown: Impact
364 on pregnancy complications]. *Gynecol Obstet Fertil Senol.* mars 2022;50(3):236-9.

- 365 28. Abu-Amara J, Szpecht D, Al-Saad SR, Karbowski LM. Contracting COVID-19 in the first and second
366 trimester of pregnancy: what we know - a concise qualitative systematic review. Arch Med Sci.
367 2021;17(6):1548-57.
- 368 29. Chen X, Huang Z, Wang J, Zhao S, Wong MC-S, Chong KC, et al. Ratio of asymptomatic COVID-19
369 cases among ascertained SARS-CoV-2 infections in different regions and population groups in
370 2020: a systematic review and meta-analysis including 130 123 infections from 241 studies. BMJ
371 Open. 7 déc 2021;11(12):e049752.
- 372 30. Tsatsaris V, Mariaggi A-A, Launay O, Couffignal C, Rousseau J, Ancel PY, et al. SARS-COV-2 IgG
373 antibody response in pregnant women at delivery. Journal of Gynecology Obstetrics and Human
374 Reproduction. 1 sept 2021;50(7):102041.

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377 **Figures legends:**

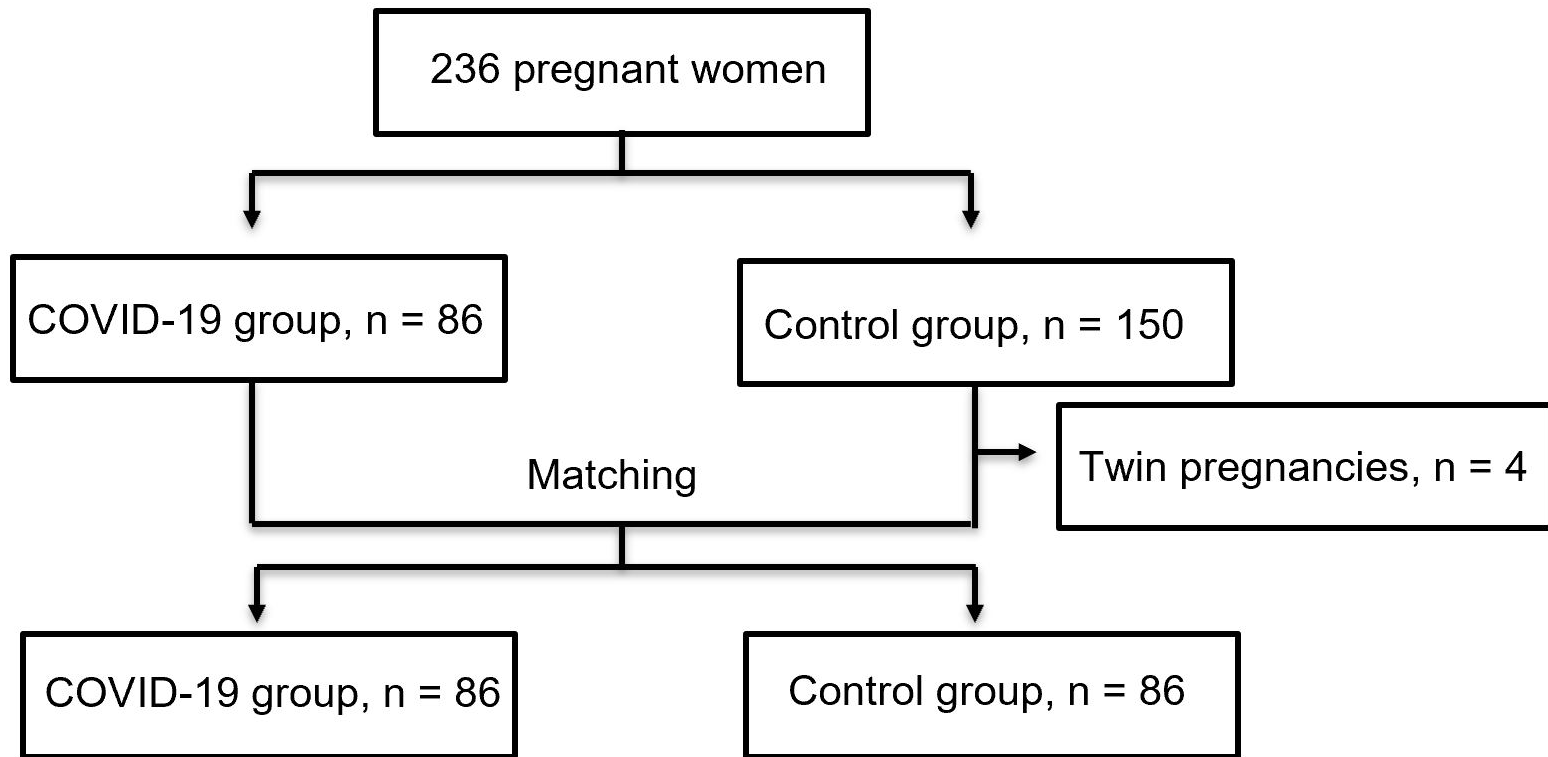
378 Figure 1: Flow chart

379 Figure 2: Color pie chart showing clinical picture and hospitalization rate

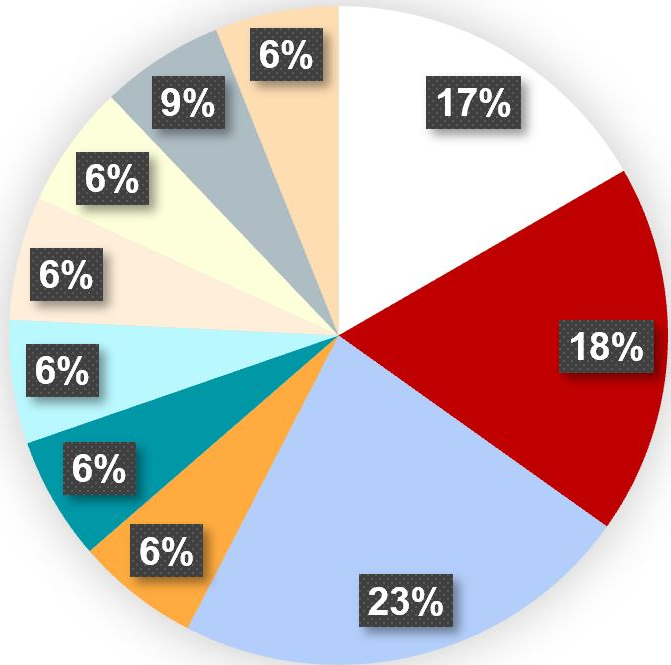
380 Figure 3: Histogram of preeclampsia, placental abruption and intra uterine death between 2019 and
381 2020 period

382

383



Symptoms



Asymptomatic

Fever

Cough

Dyspnea

Anosmia

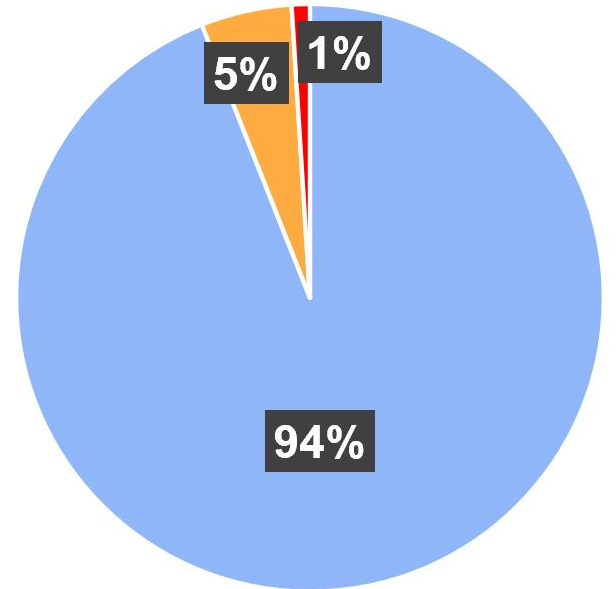
Ageusia

Diarrhea

Myalgia

Headache

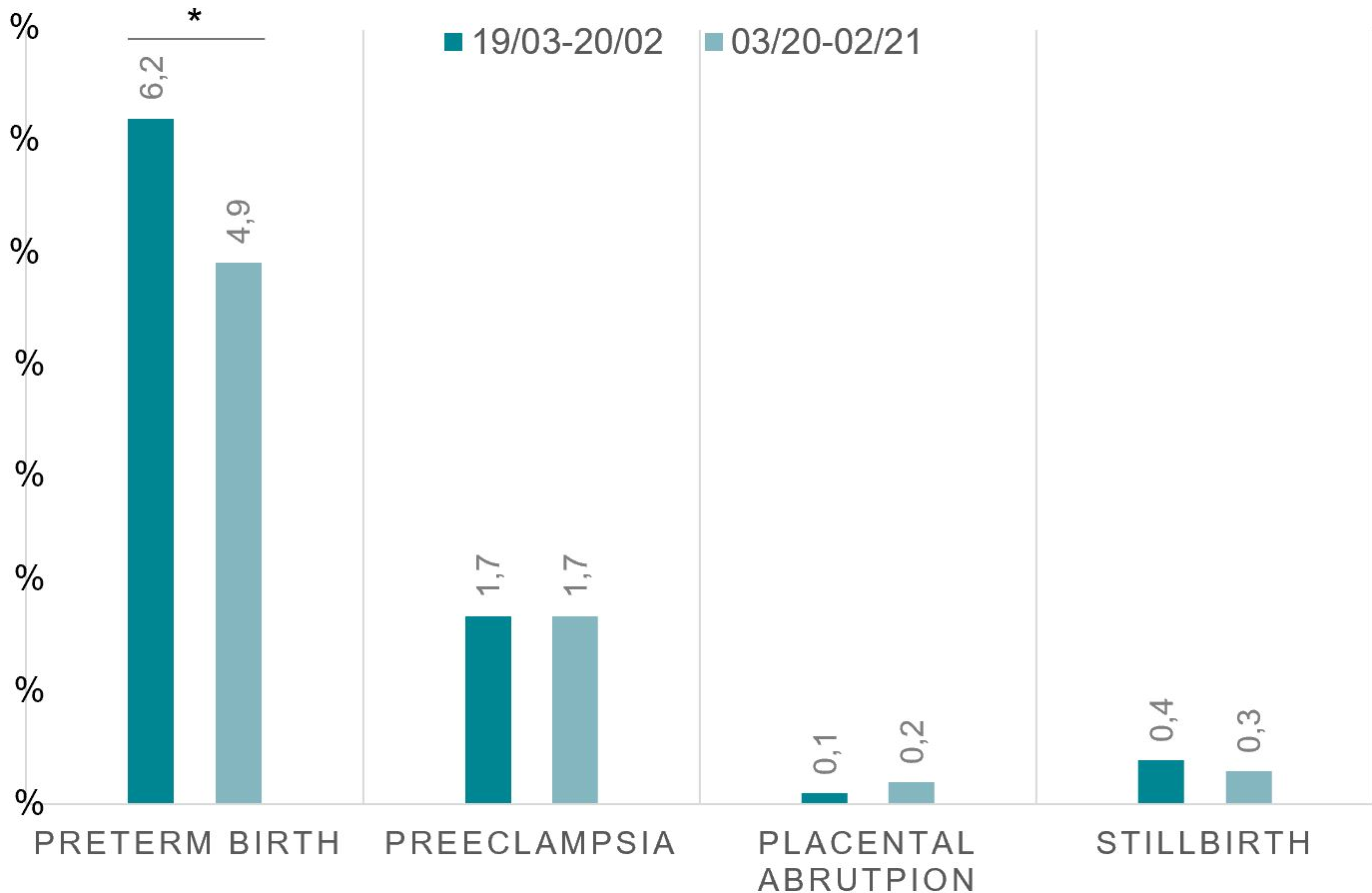
Rhinitis



No hospitalization

Hospitalization

ICU



*: p < 0.05

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 > 30 kg/m ²	n (%)	59 (72.0%) 23 (28.0%)	63 (78.8%) 17 (21.3%)	0.32
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 : 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	-