

# Journal Pre-proof



Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases

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1 **Title page**

2 **Coronavirus disease 2019 (COVID-19) in pregnant women: A report**

3 **based on 116 cases**

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38

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40

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66

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68

69 **Condensation**

70 The clinical characteristics and pregnancy outcomes in 116 pregnant COVID-  
71 19 cases in China were reported and COVID-19 during pregnancy is not  
72 associated with an increased risk of spontaneous abortion and spontaneous  
73 preterm birth.

74

75 **Short Title**

76 COVID-19 in pregnant women: 116 cases

77

78 **AJOG at a Glance**

79 A. Why was the study conducted?

- 80 • To report maternal and neonatal outcome of COVID-19 in pregnancy of  
81 116 patients.

82 B. What are the key findings?

- 83 • There were eight cases (6.9%, 8/116) of severe pneumonia but no  
84 maternal deaths.
- 85 • One of eight patients (12.5%, 1/8) that presented in the first- and early-  
86 second-trimester had a missed spontaneous abortion.
- 87 • The rate of spontaneous preterm birth before 37 weeks was 6.1% (6/99).
- 88 • Eighty-six of the 100 neonates that had testing for SARS-CoV-2 had  
89 negative results.

90 C. What does this study add to what is already known?

91 • SARS-CoV-2 infection during pregnancy is not associated with an

92 increased risk of spontaneous abortion and spontaneous preterm birth.

93 • There is no evidence of vertical transmission of SARS-CoV-2 infection

94 when the infection manifests during the third-trimester of pregnancy.

95

## 96 **ABSTRACT**

### 97 **Background**

98 The coronavirus disease 2019 (COVID-19), caused by severe acute  
99 respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global public health  
100 emergency. Data on the effect of COVID-19 in pregnancy are limited to small  
101 case series.

102

### 103 **Objectives**

104 To evaluate the clinical characteristics and outcomes in pregnancy and the  
105 vertical transmission potential of SARS-CoV-2 infection.

106

### 107 **Study Design**

108 Clinical records were retrospectively reviewed for 116 pregnant women with  
109 COVID-19 pneumonia from 25 hospitals in China between January 20 and  
110 March 24, 2020. Evidence of vertical transmission was assessed by testing  
111 for SARS-CoV-2 in amniotic fluid, cord blood, and neonatal pharyngeal swab  
112 samples.

113

### 114 **Results**

115 The median gestational age on admission was  $38^{+0}$  (IQR  $36^{+0}$ - $39^{+1}$ ) weeks.

116 The most common symptoms were fever (50.9%, 59/116) and cough (28.4%,

117 33/116); 23.3% (27/116) patients presented without symptoms. Abnormal  
118 radiologic findings were found in 96.3% (104/108) of cases. There were eight  
119 cases (6.9%, 8/116) of severe pneumonia but no maternal deaths. One of  
120 eight patients (1/8) that presented in the first- and early-second-trimester had  
121 a missed spontaneous abortion. Twenty-one of 99 patients (21.2%, 21/99)  
122 that had delivered had preterm birth, including six with preterm premature  
123 ruptured of membranes. The rate of spontaneous preterm birth before 37  
124 weeks was 6.1% (6/99). There was one case of severe neonatal asphyxia that  
125 resulted in neonatal death. Eighty-six of the 100 neonates that had testing for  
126 SARS-CoV-2 had negative results, of these ten neonates had paired amniotic  
127 fluid and cord blood samples that were tested negative for SARS-CoV-2.

128

## 129 **Conclusions**

130 SARS-CoV-2 infection during pregnancy is not associated with an increased  
131 risk of spontaneous abortion and spontaneous preterm birth. There is no  
132 evidence of vertical transmission of SARS-CoV-2 infection when the infection  
133 manifests during the third-trimester of pregnancy.

134

## 135 **Keywords**

136 Ascending infection, Coronavirus, coronavirus disease 2019, COVID-19,  
137 vertical transmission, spontaneous abortion, pandemic, pneumonia, preterm

138 birth, PTB, pregnancy outcomes, pregnancy, pregnant women, SARS-CoV-2,

139 severe acute respiratory syndrome coronavirus 2, spontaneous preterm birth,

140 spontaneous PTB, vertical transmission

141

Journal Pre-proof

## 142 **Introduction**

143 The coronavirus disease 2019 (COVID-19), caused by severe acute  
144 respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global public health  
145 emergency. Since the first case of COVID-19 pneumonia was reported in  
146 Wuhan, Hubei Province, China, in December 2019, the infection has spread  
147 rapidly to the rest of China and beyond.<sup>1-3</sup> Coronaviruses are enveloped, non-  
148 segmented, positive-sense ribonucleic acid (RNA) viruses belonging to the  
149 family Coronaviridae, order Nidovirales.<sup>4</sup> The epidemics of the two  $\beta$ -  
150 coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV)  
151 and Middle East respiratory syndrome coronavirus (MERS-CoV), have  
152 caused more than 10 000 cumulative cases in the past two decades, with  
153 mortality rates of 10% for SARS-CoV and 37% for MERS-CoV.<sup>5-9</sup> SARS-CoV-  
154 2 belongs to the same  $\beta$ -coronavirus subgroup and it has genome similarity of  
155 about 80% and 50% with SARS-CoV and MERS-CoV, respectively.<sup>10</sup> The  
156 latest report from the World Health Organization (WHO) on March 3<sup>rd</sup>,<sup>11</sup>  
157 estimated the global mortality rate of COVID-19 to be 3.4%; although recent  
158 reports that have used appropriate adjustment for the case ascertainment rate  
159 and the time lag between symptoms onset and death suggest the mortality  
160 rate to be lower at 1.4%.<sup>12</sup>

161

162 Pregnant women are particularly susceptible to respiratory pathogens and  
163 severe pneumonia, because of the physiologic changes in the immune and  
164 cardiopulmonary systems (e.g. diaphragm elevation, increased oxygen  
165 consumption, and edema of respiratory tract mucosa), which can render them  
166 intolerant to hypoxia. The 1918 influenza pandemic caused a mortality rate of  
167 2.6% in the overall population, but 37% among pregnant women.<sup>13</sup> In 2009,  
168 pregnant women were reported to be at an increased risk for complications  
169 from the pandemic H1N1 2009 influenza virus infection, with a higher  
170 estimated rate of hospital admission than in the general population.<sup>14</sup> In 2003,  
171 it was reported that around 50% of pregnant women who developed SARS-  
172 CoV were admitted to the intensive care unit (ICU), around 33% of pregnant  
173 women with SARS-CoV required mechanical ventilation, and the mortality rate  
174 was as high as 25% for these women.<sup>15</sup>

175

176 To date, data on the effect of COVID-19 in pregnancy are limited to small  
177 case series.<sup>16-20</sup> The objective of this multicenter study of 116 pregnant  
178 women with COVID-19 pneumonia is to evaluate the clinical characteristics  
179 and outcomes in pregnancy and the vertical transmission potential of SARS-  
180 CoV-2 infection.

181

182 **Materials and Methods**

### 183 **Study Design and Participants**

184 This study was reviewed and approved by the Medical Ethical Committee of  
185 Zhongnan Hospital of Wuhan University (Reference 2020004) and Renmin  
186 Hospital of Wuhan University (Reference WDRY2020-K015, WDRY2020-  
187 K016). For the collection of clinical data, verbal consent from pregnant women  
188 was obtained and written informed consent was waived in light of the urgent  
189 need to collect data. Written informed consent was obtained from pregnant  
190 women agreeing to the testing of biological samples and neonatal pharyngeal  
191 swab samples. Data were analyzed and interpreted by the authors. All the  
192 authors reviewed the manuscript and vouch for the accuracy and  
193 completeness of the data and for the adherence of the study to the protocol.  
194 The funding agencies did not participate in study design, data collection, data  
195 analysis, or writing of the report.

196

### 197 **Data Collection**

198 This was an expanded series from four previous small case series.<sup>16,18-20</sup> We  
199 obtained the medical records and compiled clinical and outcome data for  
200 consecutive pregnant women with COVID-19 pneumonia from 25 hospitals  
201 (Supplementary Material) within and outside of Hubei province, respectively,  
202 between January 20 and March 24, 2020. COVID-19 was diagnosed on the  
203 basis of the New Coronavirus Pneumonia Prevention and Control Program

204 published by the National Health Commission of China.<sup>21-24</sup> A laboratory-  
205 confirmed case of COVID-19 was defined as a positive result on quantitative  
206 reverse-transcriptase-polymerase-chain-reaction (qRT-PCR) assay of  
207 maternal pharyngeal swab specimens. At the peak of the COVID-19 outbreak  
208 within Hubei province, China, cases with relevant symptoms, significant  
209 epidemiological history and typical chest computed tomography (CT) findings  
210 were clinically diagnosed as COVID-19 pneumonia, as the viral nucleic acid  
211 test was reported to have a false-negative rate of 30%.<sup>22</sup>

212

213 Complete epidemiological history, clinical symptoms or signs, laboratory and  
214 radiologic findings, treatment measures and outcomes data were extracted  
215 from electronic medical records by a team of experienced clinicians and  
216 curated with customized data collection form. All laboratory testing and  
217 radiologic assessments, included chest CT, were performed according to the  
218 clinical care needs of the patient. Laboratory assessments consisted of  
219 complete blood count, liver and renal function, electrolytes, C-reactive protein  
220 and coagulation testing. We determined the presence of a radiologic  
221 abnormality on the basis of the documentation or description in medical charts.  
222 The date of onset of disease was defined as the day when the symptoms  
223 were noticed. The intervals from onset of disease to hospital admission and  
224 delivery were recorded. Data on pregnancy and neonatal outcome, including

225 gestational age at delivery, mode of delivery, indication for Cesarean delivery,  
226 complications, neonatal birthweight, Apgar scores and neonatal intensive care  
227 unit (NICU) admission, was collected. The date of data cutoff for outcomes  
228 was March 24, 2020. The degree of severity of COVID-19 pneumonia (severe  
229 vs. nonsevere) was defined by the Infectious Diseases Society of  
230 America/American Thoracic Society guidelines for community-acquired  
231 pneumonia.<sup>25</sup>

232

233 Two study investigators (J.Y. and J.J.) independently reviewed the data  
234 collection forms to verify data accuracy. Major disagreement between the two  
235 investigators was resolved by consultation with a third investigator (H.Y.).

236

### 237 **Sample collection**

238 Amniotic fluid samples from patients with COVID-19 pneumonia were  
239 obtained via direct needle syringe aspiration at the time of Cesarean delivery.

240 Cord blood and neonatal pharyngeal swab samples were collected  
241 immediately after delivery in the operating room or delivery room. Evidence of  
242 vertical transmission was evaluated by testing for the presence of SARS-CoV-  
243 2 in these clinical samples. In addition, vaginal secretion samples were  
244 collected from the lower-third of the vagina on admission and breast milk  
245 samples were collected at the first lactation in Zhongnan Hospital of Wuhan

246 University and Renmin Hospital of Wuhan University. All samples were  
247 processed at the State Key Laboratory of Virology/Institute of Medical Virology,  
248 School of Basic Medical Sciences, Wuhan University, and Laboratory  
249 medicine center of Renmin Hospital of Wuhan university for further testing.  
250 Sample collection, processing, and laboratory testing complied with WHO  
251 guidance.<sup>26</sup> All samples, as described above, were tested for SARS-CoV-2 by  
252 use of qRT-PCR with the Chinese CDC recommended Kit.

253

#### 254 **Study outcomes**

255 The primary end point was admission to ICU, the use of mechanical  
256 ventilation, or death. Secondary end points were the rates of spontaneous  
257 abortion, preterm delivery, Cesarean delivery and neonatal COVID-19.

258

#### 259 **Statistical Analysis**

260 Continuous variables were expressed as means (standard deviations [SD]) or  
261 medians (interquartile ranges [IQR]) or simple ranges, as appropriate.  
262 Categorical variables were summarized as counts and percentages. The  
263 results were presented in the total study population and according to the  
264 methods of diagnosis for COVID-19 pneumonia. The statistical software  
265 SPSS for Windows version 23 (SPSS, Illinois, USA) was used for data  
266 analyses.

267

## 268 **Results**

### 269 **Clinical Characteristics**

270 The characteristics and outcomes of the study population of 116 cases,  
271 including 65 cases of laboratory-confirmed and 51 cases of clinically  
272 diagnosed COVID-19 pneumonia, are shown in Table 1. The mean age was  
273 30.8 (range 24-41) years and median gestational age on admission was 38<sup>+0</sup>  
274 (IQR 36<sup>+0</sup>-39<sup>+1</sup>) weeks. In 59.5% (69/116) of cases the women reported a  
275 history of relevant environmental exposure and 32.8% (38/116) had contact  
276 with infected persons. The most common symptoms at presentation were  
277 fever in 50.9% (59/116), cough in 28.4% (33/116) and fatigue in 12.9%  
278 (15/116). In 23.3% (27/116) of cases there were no signs or symptoms of the  
279 disease; 77.8% (21/27) of which were clinically diagnosed with COVID-19  
280 pneumonia. All these 21 cases underwent investigations because of  
281 significant epidemiological history.

282

283 Notably, there were nine patients (7.8%, 9/116) with gestational diabetes, five  
284 (4.3%, 5/116) with hypertensive disorders including four (3.4%, 4/116) with  
285 preeclampsia and these pregnancy complications were unrelated to COVID-  
286 19 pneumonia. There were eight patients (6.9%, 8/116) with severe  
287 pneumonia, all requiring ICU admission, of which one (0.9%, 1/116) required

288 plasmapheresis, six (5.2%, 6/116) received non-invasive ventilation, two  
289 (1.7%, 2/116) received invasive mechanical ventilation, and one (0.9%, 1/116)  
290 received extracorporeal membrane oxygenation. Clinical details of the cases  
291 of severe pneumonia are presented in Supplementary Table. Seventy-six  
292 (65.5%, 76/116) cases had been discharged. There were no cases of  
293 maternal death.

294

295 On admission, lymphocytopenia was present in 44.0% (51/116) of the patients  
296 and leukopenia in 24.1% (28/116), according to pregnancy-specific normal  
297 ranges.<sup>27</sup> Forty-four percent of the patients had elevated levels of C-reactive  
298 protein. Patients with severe disease had more prominent laboratory  
299 abnormalities (including lymphocytopenia and leukopenia) than those with  
300 nonsevere disease. In cases that had chest CT scans at the time of admission,  
301 96.3% (104/108) revealed abnormal results. Of note, all cases of clinically  
302 diagnosed COVID-19 pneumonia had abnormal chest CT findings (Table 2).

303

#### 304 **Pregnancy Outcomes**

305 Of the 116 pregnant women with COVID-19 pneumonia, eight cases  
306 presented before 24 weeks. One case (12.5%, 1/8) was complicated with a  
307 missed spontaneous abortion at 5<sup>+2</sup> weeks at presentation with fever and  
308 fatigue. In the remaining seven ongoing cases, four had reached 20 weeks

309 and morphology scan showed normal anatomy and fetal growth. Ten cases  
310 presented between 24 and 33<sup>+6</sup> weeks, of which seven cases are ongoing,  
311 one delivered at term and two cases (20%, 2/10) had iatrogenic preterm  
312 delivery. One had a Cesarean delivery at 28<sup>+1</sup> weeks on the same day of  
313 admission for severe pneumonia; one had a Cesarean delivery at 31<sup>+6</sup> weeks  
314 on the same day of admission for twin pregnancy. Twenty-two cases  
315 presented between 34 and 36<sup>+6</sup> weeks, 19 delivered preterm, two delivered at  
316 term and one case remained undelivered. 27.3% (6/22) had preterm  
317 premature ruptured of membranes (PPROM), two cases (33.3%, 2/6) resulted  
318 in vaginal delivery; whilst four cases (66.7%, 4/6) cases required Cesarean  
319 delivery, with three cases indicated for symptomatic COVID-19 pneumonia  
320 and one because of history of previous Cesarean delivery. There are 16  
321 ongoing pregnancies; with one patient with gestational diabetes mellitus, and  
322 the other 15 patients with no fetal/maternal complications reported as of  
323 March 24, 2020.

324

325 Ninety-nine pregnant women, including one with twin pregnancy, delivered  
326 their babies during hospitalization, 85.9% (85/99) underwent Cesarean  
327 delivery and 14.1% (14/99) had a vaginal delivery (Table 3). The Cesarean  
328 delivery was indicated for COVID-19 pneumonia in 38.8% (33/85), previous  
329 Cesarean delivery in 18.8% (16/85), fetal distress in 10.6% (9/85) and failure

330 to progress in 5.9% (5/85) (Table 3). The rates of preterm delivery before 34  
331 weeks and 37 weeks were 2.0% (2/99) and 21.2% (21/99), respectively  
332 (Table 3). Among the 21 preterm deliveries, 28.6% (6/21) had PPROM and  
333 two of which resulted in vaginal deliveries. There were no cases with  
334 spontaneous onset of labor. The rate of spontaneous preterm birth before 37  
335 weeks was therefore 6.1% (6/99). No cases of spontaneous preterm delivery  
336 before 34 weeks were reported.

337

338 There were no cases of fetal deaths. Among 100 neonates, there was one  
339 case of severe neonatal asphyxia. 47.0% (47/100) neonates were transferred  
340 to NICU for further treatment (Table 3). There was one case of neonatal death.  
341 The mother of this neonate developed severe pneumonia and septic shock  
342 after admission and required ICU admission for invasive ventilation. The  
343 neonate (male) was delivered at 35<sup>+2</sup> weeks by Cesarean section and severe  
344 neonatal asphyxia was reported. He had 1-min, 5-min and 10-min Apgar  
345 scores of 1,1 and 1, respectively. He was treated with invasive ventilation and  
346 died within 2 hours of birth. As of March 24, 2020, 76.0% (76/100) neonates  
347 had been discharged and 23.0% (23/100) neonates remained in hospital  
348 (Table 3).

349

350 86.0% (86/100) of neonates were tested for SARS-CoV-2 viral nucleic acid on  
351 pharyngeal swab samples and the results were negative. Ten of these 86  
352 neonates had paired amniotic fluid and cord blood samples that were tested  
353 negative for SARS-CoV-2.<sup>16,20</sup> Six patients consented and had their vaginal  
354 secretion samples tested and were negative.<sup>20</sup> Twelve patients had their  
355 breast milk samples tested and were negative.<sup>16,20</sup>

356

### 357 **Comments**

### 358 **Principal Findings**

359 We report clinical data from 116 pregnant women with COVID-19 pneumonia.  
360 This descriptive study demonstrated that, firstly, the clinical characteristics of  
361 these patients with COVID-19 pneumonia during pregnancy were similar to  
362 those of nonpregnant adults with COVID-19 pneumonia, as previously  
363 reported;<sup>28,29</sup> secondly, 23.3% (27/116) of pregnant patients did not present  
364 with symptoms; however, the majority of these patients were diagnosed with  
365 COVID-19 pneumonia based on clinical criteria during the peak of the  
366 outbreak in Hubei Province, China; thirdly, 6.9% (8/116) of pregnant patients  
367 developed severe pneumonia requiring ICU admission and none died, as of  
368 March 24, 2020; fourthly, the rate of spontaneous abortion was 12.5% (1/8);  
369 fifthly, the rate of preterm birth before 37 weeks was 21.2% (21/99), of these  
370 one-third had PPROM giving rise to a 6.1% (6/99) spontaneous preterm birth

371 rate, and lastly, 86.0% (86/100) neonates that were tested for SARS-CoV-2  
372 viral nucleic acid on samples from the pharynx had negative results, ten of  
373 these 86 neonates had paired amniotic fluid and cord blood samples that  
374 were also tested negative for SARS-CoV-2.

375

### 376 **Clinical Implications**

377 To date, summarized data from five small series, with a total of 56 pregnant  
378 women<sup>16-20</sup> diagnosed with COVID-19 during the second- and third-trimester,  
379 demonstrated that the most common symptoms at presentation were fever  
380 and cough; two-third of patients had lymphopenia and increased C-reactive  
381 protein, and 83% of cases had chest CT scan showing multiple patches of  
382 ground-glass opacity in the lungs. The rate of preterm delivery before 37  
383 weeks was 44% and 94% of cases had Cesarean delivery. Our data is an  
384 expanded series that have included 33 published cases.<sup>16,18-20</sup> We have  
385 reported clinical, laboratory and radiologic characteristics that are similar to  
386 published pregnant and nonpregnant cases of COVID-19 pneumonia.<sup>28,29</sup>  
387 Notably, our series included cases of COVID-19 that were diagnosed by  
388 clinical criteria. The majority of these cases presented at term and all women  
389 had abnormal chest CT findings. During the peak of the COVID-19 outbreak,  
390 it was considered acceptable to not wait for repeated qRT-PCR testing in  
391 order to establish the diagnosis. In comparison to laboratory-confirmed cases,

392 there were fewer cases of severe pneumonia in those that were diagnosed  
393 clinically; the Cesarean delivery rate and neonatal outcome were similar  
394 between the two groups.

395

396 Normal pregnancy has been proposed to be a state of physiologic activation  
397 of the innate limb of the immune response. Pregnant women with acute  
398 infection were reported to display a more activated phenotype.<sup>30</sup> In our study,  
399 eight out of 116 (6.9%) pregnant women had severe COVID-19 pneumonia,  
400 which is similar to the rate of severe disease that has been reported across  
401 China.<sup>28,29</sup> This finding can be attributed to our proactive and aggressive  
402 management of diagnosed pregnant cases in order to minimize the risk of  
403 disease progression. There was a lot of unknown at the beginning of the  
404 COVID-19 outbreak and we could only base our practice on prior experience  
405 with SARS-CoV. As we encountered more and more COVID-19 cases, we  
406 adapted our management and care was provided by a multidisciplinary team  
407 including obstetricians, intensivists, obstetric anesthesiologists, virologists,  
408 microbiologists, neonatologists, and infectious-disease specialists.

409

410 It has been reported that viral pneumonia in pregnant women is associated  
411 with an increased risk of preterm birth, fetal growth restriction (FGR) and  
412 perinatal mortality.<sup>31</sup> Based on nationwide population-based data it has been

413 demonstrated that pregnant women with viral pneumonia other than COVID-  
414 19 (n=1462) have an increased risk of preterm birth, FGR and having a  
415 newborn with low birth weight and Apgar score < 7 at 5-min, compared with  
416 those without pneumonia (n=7310).<sup>32</sup> A case series of 12 pregnant women  
417 with SARS-CoV in Hong Kong, China, reported three maternal deaths, four of  
418 seven patients (57%) who presented in the first-trimester had spontaneous  
419 abortion, four of five patients (80%) who presented after 24 weeks had  
420 preterm birth and two mothers recovered without delivery but their ongoing  
421 pregnancies were complicated by FGR.<sup>33</sup> Our study has shown reassuring  
422 data that the risk of spontaneous abortion is not increased in pregnant women  
423 with SARS-CoV-2 infection from the background risk of the general  
424 population.<sup>34</sup> Our data also suggests that COVID-19 is not associated with an  
425 increased risk of spontaneous preterm birth before 37 weeks, though, the risk  
426 of any preterm birth before 37 weeks is increased. For the 15 cases of  
427 iatrogenic preterm birth, Cesarean delivery was indicated for pneumonia (n=5),  
428 twin pregnancy (n=1), transverse lie with placental praevia (n=1), previous  
429 Cesarean delivery (n=3), fetal distress (n=3), preeclampsia (n=1) and poor  
430 obstetric history (n=1).

431

432 **Research Implications**

433 One main focus of this study was to investigate the possibility of vertical  
434 transmission of SARS-CoV-2 infection. We chose to test amniotic fluid, cord  
435 blood, and neonatal pharyngeal swab samples at birth to ascertain the  
436 possibility of vertical transmission. Our results show that SARS-CoV-2 was  
437 negative in all of the above biological samples, suggesting that no intrauterine  
438 fetal infection occurred as a result of SARS-CoV-2 infection during the third-  
439 trimester of pregnancy when the time interval from clinical manifestation to  
440 delivery was up to 38 days. Our findings are in agreement with what was  
441 observed with SARS-CoV. However, two recent research letters reported on  
442 three neonates, born to women with confirmed COVID-19, that tested positive  
443 for IgG and IgM antibodies despite having a negative viral nucleic acid  
444 result,<sup>35,36</sup> raising the possibility of vertical transmission, but more data are  
445 needed. In addition, this study explored whether vaginal delivery increases  
446 the risk of mother-to-child transmission during delivery by testing the vaginal  
447 secretions of COVID-19 cases at presentation and these samples were tested  
448 negative. In this expanded series, our results further showed that breast milk  
449 samples from twelve mothers with COVID-19 tested negative for SARS-CoV-  
450 2.<sup>16</sup>

451

452 **Strengths and Limitations**

453 This is the biggest pregnant series to date. Unlike the other case series, our  
454 data were collected using a standardized methodology by a team of  
455 experienced clinicians, curated with customized data collection form and  
456 verified independently by two investigators. There are some notable  
457 limitations. First, there were only eight cases of COVID-19 pneumonia during  
458 the first- and early-second-trimester of pregnancy. Seven cases have ongoing  
459 pregnancy and we do not have complete data on the risk of congenital  
460 anomalies and FGR. Four cases have reached 20 weeks and morphology  
461 scan has shown normal anatomy and fetal growth. As the COVID-19  
462 pandemic has reached a critical stage, we believe it is important to report our  
463 pregnant cases in relation to the risk of spontaneous abortion, preterm birth  
464 and vertical transmission, without waiting for complete outcome data to be  
465 available. This will delay this publication by several months. Second, we  
466 included cases that were diagnosed based on clinical criteria in this series.  
467 According to the WHO, these cases would have been classified as probable  
468 cases of COVID-19 pneumonia. Given all clinically diagnosed cases had  
469 patchy shadowing or ground-glass opacity on chest CT and significant  
470 epidemiological exposure, we believed it was important to include these cases  
471 in the total cohort as well as present the clinical characteristics and outcome  
472 data separately from the laboratory-confirmed cases. Third, 34.5% (40/116) of  
473 the patients remained in the hospital and some outcomes were unknown at

474 the time of data cutoff. Fourth, we no doubt missed patients who were  
475 asymptomatic or had nonsevere disease and who were treated at home, so  
476 our study cohort may represent the more severe end of COVID-19. Fifth, we  
477 cannot comment on the risk of vertical transmission when the clinical  
478 manifestation to delivery interval is beyond 38 days. Sixth, only a small  
479 number of cases had vaginal secretion sample collection at presentation and  
480 breast milk samples tested for SARS-CoV-2. This study has the limitation to  
481 conclude that vaginal delivery and breastfeeding do not increase the risk of  
482 mother-to-child transmission of SARS-CoV-2. In order to explore whether  
483 there is a risk of ascending infection during labor, intrapartum vaginal  
484 secretion samples, followed by placental tissue, amniotic fluid and amnion-  
485 chorion interface swap samples should be tested for SARS-CoV-2.

486

## 487 **Conclusions**

488 In conclusion, the clinical characteristics of pregnant women with COVID-19  
489 pneumonia are similar to those of nonpregnant adults with COVID-19  
490 pneumonia. Currently, there is no evidence that pregnant women with COVID-  
491 19 are more prone to develop severe pneumonia, in comparison to  
492 nonpregnant patients. Reassuringly, the risks of spontaneous abortion and  
493 spontaneous preterm birth are not increased. There is no evidence of vertical  
494 transmission of SARS-CoV-2 when the infection manifests during the third-

495 trimester of pregnancy. Ongoing collection of clinical data and research is  
496 currently underway with the aim to answer some of the questions in relation to  
497 the risk of congenital infection, intrapartum management and mode of delivery.  
498

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499 **Author Contributions**

500 HY had full access to all of the data in the study and take responsibility for the  
501 integrity of the data and the accuracy of the data analysis. HY and DC  
502 designed the study. YZ, CF, JG, CW, XY, JL, HC, YQ, CL, DL, GX, LF, FX,  
503 WH, QP, XH, SW were responsible for data collection and confirmation. JJ  
504 and JY analyzed the data. JY and LCP were in charge of data interpretation  
505 and writing the manuscript draft. LCP and HY made substantial revisions to  
506 the manuscript. JY, JG, CF and JJ, contributed equally and share first  
507 authorship. HY, LCP, YZ, DC contributed equally to this article.

508

509 **Acknowledgment**

510 Not applicable.

511

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**Table 1: Demographics, baseline characteristics, and clinical outcomes of COVID-19 infection in pregnant women**

	All patients (n=116)	Laboratory- confirmed (n=65)	Clinically diagnosed (n=51)
<b>Age, years</b>			
Mean±SD	30.8 ± 3.8	30.3 ± 3.7	31.3 ± 4.0
Range	24.0-41.0	24.0-40.0	24.0-41.0
<b>Gestational age on admission, weeks</b>			
Median(IQR)	38.0 (36.0,39.1)	36.7 (33.8,38.4)	39.0 (38.0,39.4)
Range	5-41 <sup>+2</sup>	5-41 <sup>+2</sup>	30-41
<13 <sup>+6</sup> , n (%)	4 (3.4)	4 (6.2)	0
14-27 <sup>+6</sup> , n (%)	6 (5.2)	6 (9.2)	0
28-36 <sup>+6</sup> , n (%)	30 (25.9)	24 (36.9)	6 (11.8)
≥37, n (%)	76 (65.5)	31 (47.7)	45 (88.2)
<b>Parity</b>			
Nulliparous, n (%)	64( 55.2)	37( 56.9)	27 (52.9)
Multiparous, n (%)	52 (44.8)	28 (43.1)	24 (47.1)
<b>Epidemiological history</b>			
Relevant environmental exposure, n (%)	69( 59.5)	39 (60.0)	30( 58.8)
Contact with infected person, n (%)	38 (32.8)	26 (40.0)	12 (23.5)
<b>Symptoms</b>			
Fever <sup>a</sup> , n (%)	59 (50.9)	45( 69.2)	14 (27.5)
Cough, n (%)	33 (28.4)	28 (43.1)	5 (9.8)
Fatigue, n (%)	15 (12.9)	13 (20.0)	2 (3.9)
Shortness of breath, n (%)	9 (7.8)	8 (12.3)	1 (2.0)
Sore throat, n (%)	10 (8.6)	10 (15.4)	0
Myalgia, n( %)	6 (5.2)	5 (7.7)	1 (2.0)

Dyspnea, n (%)	3 (2.6)	3 (4.6)	0
Diarrhea, n (%)	1 (0.9)	1 (1.5)	0
No symptoms, n (%)	27 (23.3)	6 (9.2)	21 (41.2)
Pregnancy complications			
Gestational diabetes mellitus	9 (7.8)	3 (4.6)	6 (11.8)
Hypertensive disorders	5 (4.3)	2 (3.1)	3 (5.9)
Preeclampsia	4 (3.4)	1 (1.5)	3 (5.9)
Disease severity			
Severe	8 (6.9)	6 (9.2)	2 (3.9)
Non-severe	108 (93.1)	59 (90.8)	49 (96.1)
Treatment			
Antibiotic therapy	109 (94.0)	58 (89.2)	51 (100)
Antiviral therapy	63 (54.3)	48 (73.8)	15 (29.4)
Use of corticosteroid	37 (31.9)	26 (40.0)	11 (21.6)
ICU admission	8 (6.9)	6 (9.2)	2 (3.9)
Noninvasive ventilation	6 (5.2)	6 (9.2)	0
Invasive mechanical ventilation	2 (1.7)	2 (3.1)	0
ECMO	1 (0.9)	1 (1.5)	0
Plasmapheresis	1 (0.9)	0	1 (2.0)
Clinical outcomes			
Remained in hospital	40 (34.5)	24 (36.9)	16 (31.4)
Discharged	76 (65.5)	41 (63.1)	35 (68.6)
Died	0	0	0

<sup>a</sup> including postpartum fever cases. Data are n (%). Outcomes were followed up until March 24, 2020. COVID-19: coronavirus disease 2019, ICU: Intensive care unit. ECMO: Extracorporeal Membrane Oxygenation.

**Table 2: Laboratory and radiological findings of pregnant women with COVID-19 on admission.**

	<b>All Patients (n=116)</b>	<b>Laboratory- confirmed (n=65)</b>	<b>Clinically diagnosed (n=51)</b>
<b>Leucocytes</b>			
(x10 <sup>9</sup> /L; normal range <sup>a</sup> )			
median (IQR)	7.9 (5.9,10.6)	7.5 (5.2,9.8)	8.9 (6.7,11.0)
Decreased, n (%)	28 (24.1)	20 (30.8)	8 (15.7)
Normal, n (%)	85 (73.3)	42 (64.6)	43 (84.3)
Increased, n (%)	3 (2.6)	3 (4.6)	0
<b>Lymphocytes</b>			
(x10 <sup>9</sup> /L; normal range 1.1-3.2)			
median (IQR)	1.2 (0.9,1.6)	1.0 (0.8,1.6)	1.3 (1.1,1.6)
Decreased, n (%)	51 (44.0)	38 (58.5)	13 (25.5)
Normal, n (%)	64 (55.1)	26 (40.0)	38 (74.5)
Increased, n (%)	1 (0.9)	1 (1.5)	0
<b>C-reactive protein concentration</b>			
(mg/L; normal range 0-10)			
median (IQR)	9.3 (3.3,28.0)	16.6 (5.3,37.9)	5.9 (2.6,21.6)
Increased, n (%)	51 (44.0)	32 (49.2)	19 (37.3)
Normal, n (%)	53 (45.7)	24 (36.9)	29 (56.9)
<b>CT chest findings (n=108)</b>			
Patchy shadowing or			
ground-glass opacity, n (%)	104 (96.3)	53 (93.0)	51 (100%)
Negative finding, n (%)	4 (3.7)	4 (7.0)	0

<sup>a</sup>Normal range in pregnancy: first-trimester 5.7-13.6  $\times 10^9/L$ , second-trimester 5.6-14.8  $\times 10^9/L$ , and third-trimester 5.9-16.9  $\times 10^9/L$  (from *Williams Obstetrics 25<sup>th</sup> Edition*<sup>27</sup>). Data are n (%). Increased means over the upper limit of the normal range and decreased means below the lower limit of the normal range. COVID-19: coronavirus disease 2019, CT: Computed tomography.

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**Table 3: Pregnancy and neonatal outcomes of COVID-19.**

	<b>All deliveries (n=99)</b>	<b>Laboratory- confirmed (n=50)</b>	<b>Clinically diagnosed (n=49)</b>
<b>Mode of delivery</b>			
Cesarean delivery, n (%)	85 (85.9)	44 (88.0)	41 (83.7)
Vaginal delivery, n (%)	14 (14.1)	6 (12.0)	8 (16.3)
<b>Indication of Cesarean delivery<sup>a</sup></b>			
COVID-19 pneumonia, n (%)	33 (38.8)	19 (43.2)	14 (34.1)
Previous Cesarean delivery, n (%)	16 (18.8)	8 (18.2)	8 (19.5)
Fetal distress, n (%)	9 (10.6)	7 (15.9)	2 (4.9)
Failure to progress, n (%)	5 (5.9)	3 (6.8)	2 (4.9)
Preeclampsia, n (%)	4 (4.7)	1 (2.3)	3 (7.3)
Abnormal fetal growth, n (%)	2 (2.4)	0	2 (4.9)
Placenta previa, n (%)	3 (3.5)	0	3 (7.3)
Others, n (%)	13 (15.3)	6 (13.6)	7 (17.1)
<b>Onset of symptoms to delivery, days</b>			
Median (IQR)	2.5 (1.0,6.7)	4.0 (1.0-7.0)	4.0 (0.5,8.5)
Range	0-38.0	0-38.0	0-22.0
<b>Gestational age at delivery</b>			
Median (IQR)	38.4 (37.3,39.4)	38.0 (36.6,39.2)	39.0 (38.1,39.4)
Range	28.1-41.3	28.1-41.3	31.9-41.0
<34 weeks, n (%)	2 (2.0)	1 (2.0)	1 (2.0)
34-36 <sup>+6</sup> weeks, n (%)	19 (19.2)	15 (30.0)	4 (8.2)
≥37 weeks, n (%)	78 (78.8)	34 (68.0)	44 (89.8)
<b>Preterm delivery before 34 weeks, n (%)</b>			
Spontaneous labor/PPROM	0	0	0
<b>Preterm delivery before 37 weeks, n (%)</b>			
	21 (21.2)	16 (32.0)	5 (10.2)

Spontaneous labor/PPROM	6 (6.1)	3 (6.1)	3 (6.1)
Clinical outcome of neonates (n=100) <sup>b</sup>			
Neonatal birthweight (g)	3108 ± 526	3087 ± 504	3130 ± 553
Apgar 1min, Median (IQR)	9 (8,9)	9 (8,9)	9 (9,9)
Apgar 5min, Median (IQR)	10 (9,10)	10 (9,10)	10 (10,10)
Severe neonatal asphyxia, n (%)	1 (1.0)	1 (2.0)	0
Transferred to NICU, n (%)	47 (47.0)	17 (34.0)	30 (60.0)
Remained in hospital, n (%)	23 (23.0)	13 (26.0)	10 (20.0)
Discharged, n (%)	76 (76.0)	36 (72.0)	40 (80.0)
Neonatal death, n (%)	1 (1.0)	1 (2.0)	0

<sup>a</sup> N (Cesarean delivery) = 85, <sup>b</sup> Including one pair of twins. Data are n (%). Outcomes were followed up until March 24, 2020. COVID-19: Coronavirus disease 2019. PPRM: Preterm premature ruptured of membranes. NICU: Neonatal intensive care unit.



<b>Leukocyte count</b>									
(<5.9-16.9 x10 <sup>9</sup> /L)									
Lymphocyte count (10 <sup>9</sup> /L)	0.884	0.69	1.42	1.5	0.54	1.02	0.3	1.09	
Lymphopenia (<1.1 x10 <sup>9</sup> /L)	+	+	-	-	+	+	+	+	
Neutrophil count (10 <sup>9</sup> /L)	/	6.01	8.87	9.83	4.78	7.41	/	10.64	
Platelet count (10 <sup>9</sup> /L)	160	184	269	282	202	274	146	271	
CRP (mg/L)	60.8	73.63	102.8	41.2	152.4	52.74	94	41.98	
Elevated CRP (>10mg/L)	+	+	+	+	+	+	+	+	
Prothrombin time, s	/	11.6	10.3	18.5	9.8	10.9	/	11.7	
Activated partial thromboplastin time, s	/	30.7	33.4	40	31.7	24.5	/	32.5	
D-dimer, mg/L	/	3.93	1.28	/	1.31	1.94	6.54	0.68	
Elevated aminotransferase (ALT<45U/L, AST<35U/L)	+	+	+	+	-	-	+	-	
ALT(U/L)	142	51	72	181	17.6	6.9	90	17	
AST(U/L)	235	22	50	213	28.2	12.6	59	28	
Creatine kinase, U/L	/	24	32.94	638	40.18	54.62	/	23	
Creatine kinase-MB, U/L	/	9	1.59	137	19.66	13.86	/	11	
Lactate dehydrogenase, U/L	/	452	322.7	638	196.3	195.5	/	276	
Total bilirubin, mmol/L	/	7.8	19.78	123.1	6.1	1.8	19.2	14.8	
Blood urea nitrogen, mmol/L	2.3	3.4	1.52	5.5	4.21	3.35	4.44	1.24	
Creatinine, μmol/L	85	46.8	56.62	152.6	54.6	49.1	61.98	38	
Procalcitonin, ng/mL	7.29	0.89	0.89	1.56	0.222	0.122	0.05	0.31	
<b>Blood gas analysis</b>									
PH	7.41	7.27	7.41	/	/	/	/	7.42	
Lactate, mmol/L	4	3.4	/	/	/	/	/	1.8	
PaO <sub>2</sub> , mmHg	60.5	117	66	/	/	/	/	86	
PaCO <sub>2</sub> , mmHg	17.7	73	36.7	/	/	/	/	24	
<b>Confirmatory test</b>									
(SARS-CoV-2 by qRT-PCR)	+	+	+	-	+	/	+	+	
<b>CT evidence of</b>									

**pneumonia**

Bilateral distribution of patchy shadows or ground glass opacity

+ + + + + + + +

Local patchy shadows or ground glass opacity

+

**Mode of delivery**

	CS	Vaginal delivery	CS	Vaginal delivery	CS	CS	Vaginal delivery	CS
Indication for CS	Previous CS Pneumonia Septic shock	/	Previous CS Pneumonia	/	Previous CS Pneumonia	Preeclampsia Pneumonia	/	Pneumonia

**Treatment**

Oxygen support (nasal cannula)

+ + + + + + + +

Antibiotic therapy

	Piperacillin and sulbactam sodium, Imipenem	Moxifloxacin, Cephalosporin, Imipenem, linezolid, Meropenem, Polymixin B, Sulfanilamide	Moxifloxacin, Cefoperazone/Sulbactam	Moxifloxacin, Meropenem	Cefpexone/Tazobactam	Cefoperazone/Sulbactam	Azithromycin, Levofloxacin, Vancomycin	Cefamandole, Ornidazole, Cefmenoxime
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Antiviral therapy

	Oseltamivir	Ganciclovir, Arbidole, Interferon	Lopinavir, Peramivir, Arbidole, Interferon	Arbidole	Oseltamivir, Interferon	Interferon	Aciclovir, Oseltamivir, Ribavirin, Interferon	Arbidole
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Use of corticosteroid

- Methylprednisolone, Prednisone Methylprednisolone Methylprednisolone - - - Methylprednisolone

Admitted to an ICU (days)

+ 30 + 14 6 3 16 15

Non-invasive ventilation (days)

Withdrew ventilation 36 days after CS 8 6 - 6 - 3 3

Invasive mechanical ventilation (days)

11 - - - - - -

ECMO (days)

Withdrew ECMO 26 days after CS - - - - - -

Plasmapheresis

- - - + - - - -

Duration of hospitalization (days)

Remain in hospital Remain in hospital 29 16 14 4 16 15

**Pregnancy outcomes**

Gestational age at delivery (wks)	35 <sup>+2</sup>	34 <sup>+2</sup>	37 <sup>+6</sup>	36 <sup>+2</sup>	39 <sup>+1</sup>	39 <sup>+1</sup>	38 <sup>+3</sup>	28 <sup>+1</sup>
Birth weight (gram)	2700	2350	3500	2670	3750	3800	3200	1530
Preterm delivery	+	+	-	+	-	-	-	+
Low birth weight	-	+	-	-	-	-	-	+
Apgar score (1min, 5min)	1,1	9,10	9,10	8,9	10,10	10,10	9,10	8,9
Neonatal asphyxia	+	-	-	-	-	-	-	-
Transferred to NICU	+	-	-	+	-	-	-	+
Non-invasive ventilation	-	-	-	-	-	-	-	-
Invasive mechanical ventilation	+	-	-	-	-	-	-	+
Neonatal death	+	-	-	-	-	-	-	-
Neonatal outcomes	Died	Discharged	Discharged	Discharged	Discharged	Discharged	Discharged	Remain in hospital
Fetal death or stillbirth	-	-	-	-	-	-	-	-

Outcomes were followed up until March 22, 2020. COVID-19: Coronavirus disease 2019, ICU: Intensive care unit, CT: Computed tomography, PPRM: Preterm premature ruptured of membranes, NICU: Neonatal intensive care unit, ECMO: Extracorporeal Membrane Oxygenation.