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.

Table 1
Clinical characteristics of pregnant women with Covid-19, according to symptoms severity.

Characteristics	All patients (n = 88)	Non severe N = 82 (93 %)	Severe (requiring oxygen support) N = 6 (7%)
Age (IQR)	31 (28–34)	31 (28–33)	34 (32–40) **
BMI (IQR)	22.7 (21–28)	22.5 (21–27)	29.6 (27–35) *
Obesity (BMI ≥ 30)	15 (17 %)	13 (16 %)	2 (33 %)
Overweight (BMI ≥ 25) (n ;%)	36 (41 %)	31 (38 %)	5 (83 %) *
Smoking (n ;%)	3 (3.4 %)	2 (2.4 %)	1 (16.7 %)
Diabetes (n ;%)	7 (8 %)	4 (%)	3 (50 %) **
Median term at the onset of the disease (range)	27 (4–40)	27 (4–40)	26 (12–34)
Positive Covid-19 PCR (n ;%)	84 (95 %)	78 (%)	6 (%)
Positive Covid-19 (n ;%)	10 (11.4 %)	9 (%)	1 (%)
Positive Covid-19 Serology (n ;%)			
Covid-19 suggestive Chest CT (n ;%)	6 (7%)	2 (%)	4 (%)
Covid-19 features			
Fever (n;%)	44 (50 %)	40 (49 %)	4 (67 %)
Cough (n;%)	55 (63 %)	50 (61 %)	5 (83 %)
Diarrhea (n;%)	28 (32 %)	23 (28 %)	5 (83 %) *
Breath difficulties (n;%)	40 (45 %)	34 (41 %)	6 (100 %) **
Muscle aches (n;%)	50 (57 %)	46 (56 %)	5 (83 %)
Fatigue (n;%)	70 (80 %)	65 (79 %)	5 (83 %)
Nausea (n;%)	22 (25 %)	18 (22 %)	4 (67 %) *
Vomiting (n;%)	14 (16 %)	10 (12 %)	4 (67 %) **
Agueusia and/or anosmia	67 (76 %)	62 (76 %)	5 (83 %)
Disease impact on the pregnancy			
Hospitalization (n;%)	17 (19 %)	11 (13 %)	6 (100 %)***
Need for oxygen (n;%)	6 (7%)	0	100 %
Uterine contractions (n;%)	15 (17 %)	13 (16 %)	2 (33 %)
Delivery (n;%)	N = 14	13	1
Cesarean section	(36 %)	4	1

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

do not know whether the severity of the disease impacted their consenting to answer. However, the data provided in this letter represents the widest sample of Covid-19-positive pregnant women that were managed either by their family doctor, by their obstetrician, or by an online follow-up platform.

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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COVID-19 infection during the third trimester of pregnancy: Current clinical dilemmas

Dear editor,

We would like to share our clinical approaches in two cases of third-trimester COVID-19 infection from two different European countries. Both cases shared similar background characteristics but different outcome. Multidisciplinary considerations and clinical dilemmas that COVID-19 and pregnancy presented to clinical practice have been comprehensively reviewed in the discussion.

Patient A. A 38-year old woman with diet controlled gestational diabetes was admitted at 31 + 6 weeks with cough, dyspnea and oxygen desaturation (Table 1). Oxygen support and molecular weight heparin (LMWH) was started and nasopharyngeal swab was found negative for SARS-Cov-2. Because of high suspicion of COVID-19 infection, a CT scan was performed and showed bilateral ground glass opacities suggestive of COVID-19

Table 1
Patient characteristics.

		Patient A	Patient B
Hospital, country		Medisch Spectrum Twente, The Netherlands	National Maternity Hospital, Ireland
Age (years)		39	29
Ethnicity		Caucasian	African
Parity		1 + 0	3 + 1
Gestation at admission (weeks)		31 + 6	40 + 0
Previous medical history		Gestational diabetes BMI 46	Chronic hepatitis B infection BMI 40 Previous C-section
Symptoms		4-day dry cough and increasing dyspnea, thoracic pain with deep breathing	1-week history of productive cough, sore throat and diarrhea
Parameters at admission	**T (°C)**	37.3	39.4
	RR (bpm)	38	18
	O2 sat (%)	94 on 3 Liter of oxygen	100 on room air
	BP (mmHg)	114/59	112/74
	HR (bpm)	94	128
Imaging		CT scan: bilateral patchy ground glass opacities (Fig. 1)	RX thorax: normal
Blood samples		↑ CRP ↑ LDH ↑ Glucose	↑ CRP
Treatment	**O2 support**	Yes	Yes
	Medication	Hydroxychloroquine	Co-amoxiclav and clarithromycin
	LMWH	During all hospitalisation	10 days postpartum
Pregnancy outcome		Day 2 and 3 betamethasone administered and further conservative management	Day 0 C-section because of maternal sepsis and fetal tachycardia: healthy male infant with Apgar 9/9
Discharge (days from admission)		day 6	day 2
SARS-Cov-2 swabs		day 0 negative day 1 positive	day 4 positive

T, Temperature; RR, Respiratory rate; BP, Blood pressure; HR, Heart rate; CRP, C-reactive protein; LMWH, Low molecular weight heparine.

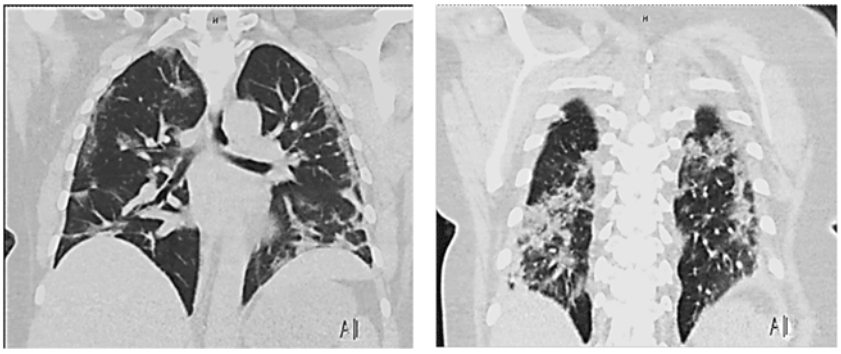

Fig. 1. CT scan on day 2 of patient A: Bilateral patchy ground glass opacities (GGO).

pneumonia (Fig. 1). Later the same day, second sample of PCR swab came back positive for SARS-Cov-2. After a multidisciplinary meeting, antenatal corticosteroids for fetal lung maturation were administered in order to optimize the fetus' state if a preterm cesarean section would be required because of sudden maternal respiratory deterioration. Hydroxychloroquine was also commenced. On day 5, we observed a rapid improvement of patient's symptoms, oxygen support was no longer needed and patient was discharged home.

Patient B. A 29-year old self-presented at 40 weeks gestation with cough, sore throat and diarrhea (Table 1). Swab for SARS-CoV-2 was pending and chest X-ray showed no signs of consolidation. Following multidisciplinary discussion, a cesarean delivery was performed in view of maternal fever, fetal tachycardia and previous cesarean section. A live male infant was delivered with Apgar of 9 and 9 and no signs of fetal distress. On day 2 of hospitalization patient was afebrile and discharged home with thromboprophylaxis. On day 4 post-delivery, SARS-CoV-2 swabs returned as positive. The baby did not develop respiratory symptoms.

Discussion

Hereby we discuss our clinical managements and multidisciplinary considerations concerning time of delivery, use of antenatal corticosteroids and thromboprophylaxis.

Time of delivery

When dealing with a critically ill patient, the question arises whether or not delivery of the infant would improve maternal outcome. For both our cases, a multidisciplinary discussion was held for this purpose and led to the administration of antenatal corticosteroids in case A (preterm) and to an emergency cesarean section in case B (term).

In the literature, reports on non-COVID-19 ARDS suggest a high mortality rate, of almost one third amongst pregnant and postpartum women [1], however it is still unclear whether delivery could significantly improve maternal outcome [1–3].

Previous studies reported an increased maternal morbidity in pregnant women compared to non-pregnant women, though no significant difference in mortality has been found [2,4]. In a retrospective review of 29 mechanical ventilated pregnant women, only a modest improvement in maternal respiratory function was seen after delivery of the infant [3].

A number of further practical factors need to be considered. First of all, the risk of a failed endotracheal intubation is eight times higher during pregnancy due to airway edema, anatomic changes and increased weight [5]. This was considered in both our patients with type III obesity. Secondly, emptying of the uterus could constitute an advantage by reducing oxygen consumption and by allowing prone positioning and a wider range of therapies without concern for fetal wellbeing. Moreover, perinatal deaths in third-trimester pregnant patients with ARDS has been reported in up to 23% [1].

To conclude, appropriate management should be evaluated on a case by case basis, according to maternal status, gestational age and maternal prognosis [6,7]. The main goal of obstetric specialists should be thus finding a subtle balance between maintaining adequate maternal saturation (PaO2 > 70 mmHg equivalent to oxygen saturation >95%) [8] and minimizing the risks of iatrogenic preterm birth and emergency cesarean section. These last two points should be emphasized as a high rate of preterm births and cesarean sections in patients with COVID-19 has been recently reported [9].

Antenatal corticosteroids

In the light of a recent meta-analysis reporting preterm births in 41% of COVID-19 infections, use of antenatal corticosteroids constitutes a second relevant and debated topic. In fact, steroids are not recommended in COVID-19 infection outside of clinical trial because of potential increased risk of mechanical ventilation [10]. However, literature solely refers to the standard use of steroids in non-pregnant patients with different dosages and duration of treatment than those standardly used for fetal indication [11].

Neither observational studies nor case-reviews on corticosteroids for fetal indication in COVID-19 have been published. To our knowledge, we are the first to report a case of COVID-19 pneumonia where a short course of antenatal corticosteroids was administered for fetal indication. Although steroids administration led to an exacerbation of pre-existent gestational diabetes, a favorable maternal outcome was observed without aggravation of her COVID pneumonia.

To sum up, no clear evidence of harm has been reported so far and antenatal corticosteroids in COVID-19 have been advised when usually offered by the Royal College of Obstetricians and Gynaecologists and certainly for delivery prior to 34 [6]. Similarly, American College of Obstetricians and Gynecologists recommended administration of corticosteroids until 33 + 6 weeks because of the well-established benefit on neonatal morbidity and mortality [7].

Thromboprophylaxis

In our case series, thromboprophylaxis was promptly started from day 1 in case A, and postpartum in case B.

Current belief is that Covid-19 immune response may cause a procoagulant state re-named COVID-19-associated coagulopathy (CAC), which has been associated to increased mortality and suggested as major pathogenic factor of SARS-CoV-2 [12]. Considering that pregnancy constitutes itself a prothrombotic state [13], pregnant patients would constitute a high-risk population in this context.

Heparin besides its anticoagulant effect could also present an anti-inflammatory and antiviral effect by binding the S-protein of SARS-CoV-2 and its use has been recently associated with increased survival [14].The American Society of Hematology has therefore recommended LMWH prophylaxis for COVID-19 patients, unless of actively bleeding or with severe thrombocytopenia [15,16].

The use of LMWH in pregnant women is broadly implemented in standard care. These considerations therefore constitute an argument to treat pregnant women with prophylactic LMWH once COVID has been diagnosed [13].

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Consent

Patient's consent has been obtained for publishing this case series.

Declaration of Competing Interest

The authors report no conflict of interest

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Is termination of early pregnancy indicated in women with COVID-19?

Dear editors,

By May 11, 2020, more than 84,430 confirmed cases and 4 suspected cases infected with 2019 novel coronavirus disease (COVID-19) have been reported in China. Besides the human-to-human transmission via respiratory droplet, vertical transmission has been concerned and not determined since one case of a mother and neonate was laboratory-confirmed with COVID-19. We studied 13 COVID-19 infected pregnant women from Renmin Hospital of Wuhan University, Wuhan, Hubei province, China and published online [1]. One woman in that study experienced the biochemical pregnancy. It is unclear whether the biochemical pregnancy was associated with maternal infection, and therefore additional research is warranted. However, several days ago, a news program of Hubei TV suggested that early pregnant women infected with COVID-19 should terminate their pregnancies. This viewpoint seems oversimplified but has triggered controversy widely. In February, there were 3 pregnant women with mild COVID-19 infection in a hospital of Wuhan who decided to terminate their pregnancy in the first trimester.

Early pregnancy is a challenging and vulnerable period, and viral infection at this stage could potentially affect embryogenesis and fetal organ development, but there is still no evidence for the vertical transmission of COVID-19 so far. In February 13rd, 2020, Chen et al. reviewed nine cases of COVID-19 infected pregnant women, and reported none of their neonates had been infected through vertical transmission [2]. Prior to COVID-19, there were a total of six coronavirus species that induced human infection including severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) which led to the outbreak of pneumonia, but no vertical transmission of the coronavirus had been confirmed [4,5]. With reference to the experience to SARS or MERS, they can cause preterm, miscarriage, stillbirth, and fetal growth restriction in pregnant women, associated with placental insufficiency, but not vertical transmission. There is no evidence that SARS-CoV or MERS-CoV itself can cause fetal malformations, because neither of them passes across the placental barrier [3,4]. Children born to pregnant women infected with SARS showed similar physical and mental development when followed up to 10 months in both full-term and preterm babies. Current research on long-term health of pregnant women of SARS or MERS is not available, but we anticipate that maternal SARS-CoV-2 infection would not result in significant, long-term health risks to the offspring.

Pregnant women with SARS-CoV infection have a three times higher mortality rate than non-pregnant populations. However, SARS-CoV-2 infection outcome seems to have a better prognosis than SARS-CoV infection [5]. Only 7.45 % of all confirmed cases are defined as “severe” according to an announcement by National Health Commission of China on Feb 15th, 2020. Based on the limited number of cases reported, there is no evidence indicating a worse outcome of maternal patients than that of general population. On the other hand, pregnancy terminations in early pregnancy may result in post-abortion infection, which might aggravate the maternal COVID-19 illness. Therefore, consideration of termination of pregnancy has to be individualized during this COVID-19 outbreak. For pregnant patients with mild symptoms, treatment should be modified to avoid using teratogenic drugs near the fetus. Patients are commonly at higher oxygen demand during early pregnancy, so hypoxemia should be monitored, and interventions should be provided without delay. For severe patients during early pregnancy, the first priority is to ensure maternal safety. Decisions of early pregnancy termination should be considered upon risk factors including viral load, transmission generations, range of lung lesions by CT (more than two lobes), maternal age, and coexisting disorders (diabetes, cardiovascular diseases etc.).

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.

Contribution to authorship

He-feng Huang put forward the initial ideas and opinions, which were drafted by Yan-ting Wu, Cheng Li, and Chen-jie Zhang.

Ethics approval

Not applicable.

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