

**SARS-COV-2 IN THE CONTEXT OF PAST CORONAVIRUSES EPIDEMICS:  
CONSIDERATION FOR PRENATAL CARE.**

Valentine Lambelet<sup>1</sup>, Manon Vouga<sup>1</sup>, Léo Pomar<sup>1</sup>, Guillaume Favre<sup>1</sup>, Eva Gerbier<sup>1,2,3</sup>, Alice Panchaud<sup>2,3,4</sup>, David Baud<sup>1</sup>

<sup>1</sup> Materno-Fetal and Obstetrics Research Unit, Department “Woman-Mother-Child”, Lausanne University Hospital, Lausanne, Switzerland.

<sup>2</sup> Center for Research and Innovation in Clinical Pharmaceutical Sciences, Institute of Pharmaceutical Sciences of Western Switzerland, Lausanne University Hospital and University of Lausanne, University of Geneva, Switzerland

<sup>3</sup> Service of Pharmacy, Lausanne University Hospital, Lausanne, Switzerland.

<sup>4</sup> Institute of Primary Health Care (BIHAM), University of Bern, Switzerland

**\*Corresponding author:**

Prof David Baud, MD PhD

Materno-fetal & Obstetrics Research Unit

Department of Obstetrics and Gynecology

Centre Hospitalier Universitaire Vaudois (CHUV)

1011 Lausanne - SWITZERLAND

Phone: (00) 41 79 556 13 51

Email: david.baud@chuv.ch

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/pd.5759

## **DISCLOSURES**

All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

## **FUNDING**

None

## STATEMENTS

**What is already known about the topic?** The emergence of severe-acute-respiratory-syndrome coronavirus 2 (SARS-CoV-2) and its consequences during pregnancy have led to an increasing volume of data about the maternal and fetal outcomes of SARS-CoV-2 infections.

**What does this study add?** This review summarizes maternal and fetal outcomes found in the literature as of April 22, 2020. This review also provides an overview of current candidate therapeutic options during pregnancy and clinical guidelines for prenatal management of COVID-19 affected pregnancies.

Data Availability Statement: Research data are not shared.

**Short title:** Coronaviruses and pregnancies

**Keywords:** Coronavirus, MERS, SARS-CoV, COVID-19, pregnancy, adverse maternal outcomes

## ABSTRACT

Since December 2019, the novel SARS-CoV-2 outbreak has resulted in millions of cases and more than 200,000 deaths worldwide. The clinical course among non-pregnant women has been described but data about potential risks for women and their fetus remain scarce. The SARS and MERS epidemics were responsible for miscarriages, adverse fetal and neonatal outcomes and maternal deaths. For COVID-19 infection, only 9 cases of maternal death have been reported as of April 22, 2020 and pregnant women seem to develop the same clinical presentation as the general population. However, severe maternal cases, as well as prematurity, fetal distress and stillbirth among newborns have been reported. The SARS-CoV-2 pandemic greatly impacts prenatal management and surveillance and raise the need for clear unanimous guidelines. In this narrative review, we describe the current knowledge about coronaviruses (SARS, MERS and SARS-CoV-2) risks and consequences on pregnancies and we summarize available current candidate therapeutic options for pregnant women. Finally, we compare current guidance proposed by RCOG, ACOG and the WHO to give an overview of prenatal management which should be utilized until future data appear.

## INTRODUCTION

In December 2019, multiple cases of pneumonia of unknown origin were reported in the Province of Wuhan, China and rapidly attributed to a novel coronavirus, closely related to the 2003 severe acute respiratory syndrome (SARS-CoV) and therefore named the severe acute respiratory syndrome 2 (SARS-CoV-2). This new virus spread throughout China and rapidly covered the globe causing over 2 million cases and more than 200,000 deaths within the recent months. The World Health Organization (WHO) declared this outbreak a pandemic on March 11, 2020 (Figure 1).

Although numerous reports have described the clinical course of COVID-19 among non-pregnant patients, data regarding pregnant women remain scarce (1)(2). Recent outbreaks of emerging infections have highlighted their potential impact on pregnant women and/or their fetus, such as the 2009 H1N1 influenza pandemic (3) or more recently, the Zika virus outbreak in the Americas (4). As information regarding this novel coronavirus is lacking, data on SARS-CoV-1 (2003) and MERS-CoV (Middle East respiratory syndrome, 2012) may help us understand the potential risks for pregnancy in the context of COVID-19. In this narrative review, we described the current knowledge (up to April 22, 2020) about the risks and consequences of SARS-CoV-2 on pregnant women and their babies and compare them to SARS and MERS. Because therapeutic options and clinical management remain unclear, we summarize information about treatments that have been tried or could be considered for COVID-19 affected pregnancies. Finally, we compare current guidelines proposed by the RCOG, ACOG and WHO to give an overview of prenatal management which should be utilized until future data are available.

## METHODS

A PubMed search was carried out using the terms “Coronavirus 2 and pregnancy”, “SARS-CoV-2 and pregnancy”, “SARS and pregnancy” and “MERS and pregnancy” that identified 447 articles published before April 22, 2020 (Figure 2 & 3). We reviewed all titles and abstracts when available, and limited the search to articles reporting maternal infections, fetal and perinatal outcomes and clinical management. Guidelines providing recommendations for management of COVID-19 pregnancies were also included. At least two reviewers evaluated the articles and extracted data. Searches were limited to the English language. The process of article selection and the number of articles are described figure 3.

## BACKGROUND: VIROLOGY AND EPIDEMIOLOGY OF EMERGING CORONAVIRUSES

*Coronaviridae* is a large family of single-stranded RNA, non-segmented and enveloped viruses. Though most of them cause benign disease, we have recently experienced the emergence of three novel coronaviruses associated with alarmingly high mortality rates: the Severe Acute Respiratory Syndrome Coronavirus 1 (SARS-CoV-1) in 2003, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2011 and most recently the SARS-CoV-2 in 2020.

These viruses are members of the *betacoronavirus* genus and have all arisen from animal reservoirs (i.e. zoonosis), namely bats for SARS-CoV and SARS-CoV2, and camels for MERS-CoV. The newly acquired human-to-human transmission allowed for their rapid dispersion, causing epidemics and pandemics among naïve populations (5). Human-to-human transmission

Accepted Article

occurs via droplets and fomites. Though transmission through aerosols has been demonstrated in laboratory conditions (6), its public health relevance remains highly debated. Recent data have demonstrated the efficacy of contact and droplet protection measures among hospitalized staff, suggesting the lack of significant aerosol transmission. (7)

SARS-CoV-1 presented as a novel atypical pneumonia in Hong Kong in June 2003. More than 8,000 individuals were infected around the world and the overall case fatality rate (CFR) was estimated to be around 11% according to the WHO (8). Drastic infectious disease control measures halted the epidemic and no cases have been reported since 2004 (5).

Later in 2012, MERS-CoV emerged in the Middle East. Infected individuals exhibited a severe respiratory illness with a high fatality rate of 34.4%. At the end of November 2019, more than 2,400 confirmed cases were reported, the majority in Saudi Arabia. This epidemic was marked by a high rate of nosocomial transmission with 19.1% of cases being healthcare workers (9).

At the end of 2019, the first cases of SARS-CoV-2 were reported in Wuhan, a large city in Southern China, and were linked to the Huanan seafood market. Early Chinese data showed an exponential growth of the number of cases suggesting human-to-human transmission among close contacts (10). The World Health Organization (WHO) declared this outbreak a pandemic on March 11, 2020 and strict measures, such as social distancing and public health hygiene protocols, have been taken by many countries to limit the spread of the disease. In many countries, the pandemic is still in its exponential phase as of May 2020.

SARS-CoV-2 causes an illness quite similar to the other emerging coronaviruses and was renamed “COVID-19” by the WHO on February 11, 2020. Typical symptoms of COVID-19 pneumonia include fever, dry cough, anosmia and fatigue. These mild presentations represent

81% of cases according to a large Chinese report of 72,134 cases (11), while 14% and 5% of cases present with severe or critical disease such as respiratory failure, septic shock, multiple organ dysfunction respectively. Similar data have been reported in the United States, with 14.3% of patients requiring intensive care management and a mortality rate that has reached 21% among hospitalized patients (12). The most frequent complications during hospitalization are acute respiratory distress syndrome (ARDS), arrhythmia and shock, as well as thromboembolic diseases (13,14). Atypical SARS-CoV-2 symptoms, such as diarrhea and nausea, have been frequently reported (15) along with neurological symptoms and complications such as Guillain-Barré (16). In addition, there are increasing reports of asymptomatic infections (17)(18). This further complicates the calculation of exact mortality rates (19,20). In a recent model based analysis, the case fatality rate was estimated to be 0.32% [0.27–0.38%] in patients <60 years old (y.o.), 6.4% [5.7–7.2%] in older patients, reaching up to 13.4% (11.2–15.9%) in those > 80 y.o (21). Comorbid conditions, such as cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer, have been shown to be associated with increased mortality (10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension and 5.6% for cancer) (11).

## **IMPACT OF EMERGING CORONAVIRUSES IN PREGNANCY**

Current data regarding emerging coronaviruses and their impact in pregnancy are mostly based on case reports and small case series. As these are often biased by worse maternal and fetal outcomes, the subsequent section should be interpreted with caution.



## Maternal outcomes

Respiratory infections are known to be associated with an increased risk of maternal complications. This was observed during the Influenza A pandemic in 2009, where up to 23% of affected women required admission to intensive care and 8.2% of them died (3,22). The relative immunosuppressed state as well as the restricted respiratory capacity of pregnancy account for such outcomes (23). Current data regarding emerging coronaviruses, based mostly on case series, are summarized below.

**SARS-CoV-1.** A total of 25 cases of SARS-CoV-1 infection among pregnant women were identified in the literature (24–30). Infections were observed in the first trimester (n=7), second trimester (n=4) and third trimester (n=14). Among the 25 cases of SARS-CoV, 3 maternal deaths (12%) were recorded, 10 patients required ICU admission (40%) with or without mechanical ventilation. Compared to non-pregnant women, the rates of ICU admission and maternal death were significantly higher and independent of the trimester of infection, including 2 patients in their first trimester. In one case, SARS-CoV-1 RNA was amplified within the cerebrospinal fluid and associated with seizures suggesting encephalitis (26).

**MERS-CoV.** 12 cases of MERS-CoV infection among pregnant women were identified in the literature. Infections occurred in all trimesters of pregnancy (n=2 for 1<sup>st</sup> trimester, n=3 for 2<sup>nd</sup> trimester and n=6 for 3<sup>rd</sup> trimester). Three (40%) maternal deaths were identified, 7 (58.3%) required ICU admission and 2 (16.7%) patients remained asymptomatic. Complications were only observed among patients in their late 2<sup>nd</sup> or 3<sup>rd</sup> trimester. No severe adverse maternal

outcomes were observed among patients infected earlier in pregnancy. The fatality rate of MERS-CoV in pregnancy (36%) was similar to non-pregnant adults (35%) (31,32,34–38).

**SARS-CoV-2.** As of April 22, 2020, more than 150 cases have been reported. We identified four cohort studies, including 118 (39) and 116 (40) Chinese patients, 42 Italian patients (41) and 43 American patients (42), respectively. Almost all infections occurred in the 3<sup>rd</sup> trimester or close to delivery. In general, pregnant women experienced symptoms similar to those of non-pregnant patients, developing mild clinical symptoms in the majority of cases with mainly fever, cough and myalgia. Interestingly, among the American cohort, 32.2% (n=14/43) of patients were asymptomatic at the time of diagnosis. Six patients remained asymptomatic after positive testing, suggesting the possibility of completely asymptomatic disease, which supports the eventual need for routine screening (43).

Severe cases of COVID-19 infection in pregnant women are not frequent as with the previous coronavirus infections described above. Nevertheless, nine (2.7%) maternal deaths have been reported among eleven Iranian patients with 3<sup>rd</sup> trimester infections (44–46). All women presented with typical symptoms, including dyspnea. They were previously healthy except two patients known for hypothyroidism and one patient with suspected gestational diabetes. Maternal age was between 22 and 49 y.o. and two women had dichorionic/diamniotic twin gestations. All women were admitted to the ICU, intubated and ventilated and died from cardiopulmonary collapse or multiple organ failure (MOF). One had septic shock and disseminated intravascular coagulation (DIC) before progressing to heart failure. Intrauterine fetal death (IUFD) were described among four patients (4/9) with gestational ages between 24

and 30 WG. CS were performed in other cases (5/9) with gestational age between 30 and 38 WG.

Cohort studies have reported a rate of severe disease requiring ICU admission of 6.9-8% (n=9/118; n=8/116), including 3 requiring mechanical ventilation among Chinese patients. In the Italian cohort, a total of 17% of pregnant women (n=7/42) required either oxygen supplementation through continuous positive airway pressure (CPAP) or ICU admission, while in the American cohort, 4 (9.3%) presented with severe disease and 2 (4.7%) required ICU admission without mechanical ventilation.

Severe complications in pregnant women are similar to what has been described in the general population and include multiple organ failure, respiratory failure requiring mechanical ventilation, and even Extracorporeal Membrane Oxygenation, as described in a patient at 35 WG (47). In the latter, the patient required an emergency cesarean section for maternal resuscitation and the newborn unfortunately died due to an intrauterine asphyxia. The mother had multiple organ failure, needed mechanical ventilation before Extracorporeal Membrane Oxygenation for a total of 7 days. She was discharged from hospital 6 weeks later.

Two cases of cardiomyopathy related to COVID19 were reported by Juusela *and al.*(48). The first pregnant woman was 45 y.o., had a BMI of 44.6 m<sup>2</sup>/kg and was diagnosed with diet-controlled gestational diabetes. She delivered via cesarean at 39 WG for severe preeclampsia and tested positive to SARS-CoV-2 on postpartum day 1 with evidence of fever, tachypnea and suspicious chest imaging. She was then diagnosed with acute heart failure after an echocardiogram was performed, showing a moderately reduced left ventricular ejection fraction (LVEF) of 40% with global hypokinesis. On day 5 postpartum, the mother required

mechanical ventilation and was still intubated at the time of publication. The second patient was a 26 y.o. women with no relevant medical history. She was admitted for respiratory symptoms necessitating nasal oxygen support. Due to the previous experience, an echocardiogram was completed and showed a moderately reduced LVEF of 40-45% with global hypokinesis. She rapidly developed severe features leading to a cesarean section at 34 WG. At the time of publication, she was postpartum day 1 and did not require oxygen support.

Though current data suggest that most pregnant women with COVID-19 will have an uncomplicated clinical course, severe complications must be anticipated. Nevertheless, the observed rates appear similar to those for non-pregnant patients between 20-40 years old. In a recent analysis based on a Chinese cohort, the actual rate of severe disease was 173/1170 (9.8%) among 20-39 y.o. patients; after adjusting for demographic factors, the expected rate of severe disease was 0.6-8.6% (21).

Breslin *et al.* also reported a similar rate of complications in pregnant women compared to non-pregnant adults (11): 86 vs 80 % with mild clinical symptoms, 9.3 vs 15 % with severe symptoms and 4.7 vs 5% requiring ICU admission respectively. We should point out, however, that complications in the general population mainly impacted the elderly and patients with comorbidities. When comparing pregnant woman to their typical age group, they qualify as a high-risk group for adverse maternal outcomes (49).

Therefore, although the majority of infected pregnant women seems to demonstrate a mild clinical course, pregnancies should be approached with caution considering the potential critical complications reported in several cases published so far report. More exhaustive data, however,

are needed to understand the additional risk pregnancy may pose to women with a COVID-19 infection.

### **Fetal and neonatal outcomes**

SARS-CoV-1 and MERS-CoV infections during pregnancy were associated with adverse fetal and neonatal outcomes.

**SARS-CoV-1.** A report on twelve pregnant women suffering from SARS-CoV-1 (2002-03 pandemic) was published (50) and the rate of adverse fetal / neonatal outcomes was 66% (8/12) in this series. Four of the seven patients (57%) infected during the first trimester experienced miscarriages. Two others decided to terminate their pregnancy after recovering from SARS, and the last had an uncomplicated pregnancy. Among the five patients infected during the second or third trimester, four (4/5, 80%) had a preterm delivery, including one for fetal distress (1/5, 20%). Two neonates exhibited respiratory distress syndrome and other complications related to prematurity (necrotizing enterocolitis). All placentas of these patients (5/5, 100%) weighed below the 5<sup>th</sup> percentile, of which 2 had abnormal anatomic-pathology results (thrombotic vasculopathy with avascular fibrotic villi and / or placental infarct) (51). When the infection occurred during the week before birth, no fetal growth restriction was noted (0/2). When the infection occurred one month or more before birth, two fetuses (2/3, 33%) had fetal growth restriction (FGR) with oligohydramnios, related to the abnormal placentas presented above. Another Chinese series (52) reported fetal demise in one of five (20%) fetuses exposed to SARS-COV-1 during the second or third trimester of pregnancy.

**MERS-CoV.** Eleven fetuses / neonates from mothers infected with MERS-CoV have been described (53)(54)(55). Among them, 3 (3/11, 27%) had fetal or neonatal demise: two intra-uterine fetal deaths at 20 and 34 weeks, and one neonatal demise at 24 weeks due to extreme prematurity (55)(56). Abruption was identified on placental examination from these fetuses, and from another liveborn neonate who presented with fetal distress at 37 weeks (57).

**SARS-CoV-2.** With regards to SARS-CoV-2 infection during pregnancy, several case-series and case reports show that similar adverse fetal and neonatal outcomes could occur. Overall, we included 142 cases with fetal and/or neonatal outcomes available at the time of this review. Among them, 40 (28%) were born prematurely (<37w) and 20 (14%) had adverse outcomes (FGR, fetal or neonatal demise, severe symptoms at birth). Congenital or perinatal transmission was suspected in 6 of 115 (5%) newborns tested. Details of all cases available are presented in Table 1.

In a case-control study (58), among 17 fetuses from SARS-CoV-2 infected mothers, 3 exhibited FGR (3/17, 18%), 2 had fetal distress (2/17, 12%), and four were born prematurely (4/17, 24%) due to PROM or placental bleeding. The rates of low birth weight and premature birth were significantly higher when compared to the control groups. One of these fetuses also exhibited sinus tachycardia that persisted after birth. Zhu and colleagues (59) described the outcomes of 10 neonates from SARS-CoV-2 infected mothers. Two of them were small for gestational age (2/10, 20%), and 6 had a Pediatric Critical Illness Score (PCIS) below 90 with shortness of breath (6/10, 60%), fever (2/10, 20%), thrombocytopenia accompanied by abnormal liver

function (2/10, 20%), tachycardia (1/10, 10%), vomiting (1/10, 10%), and pneumothorax (1/10, 10%). Neonatal radiography showed abnormalities in 7 of them (7/10, 70%): 4 had signs of infection, 2 respiratory distress syndrome and 1 pneumothorax. Among these neonates, two (2/10, 20%) had disseminated intravascular coagulation and one (1/10, 10%) refractory shock with multiple organ failure leading to death at day 8 of life. Liu Y. (60) presented the outcomes of 10 other newborns exposed during pregnancy: none which were positive for SARS-CoV-2 at birth, 6 (6/10, 60%) were premature (for fetal distress in 3 cases, 3/10, 30%), and one was stillborn (1/10, 10%). Chen and colleagues (61) described a series of 9 newborns from infected mothers during the third trimester. Two (2/9, 22%) had a low birthweight and four (4/9, 44%) were premature (for fetal distress in 2 cases), none experienced a severe adverse outcome. Yu and colleagues also reported a series of 7 newborns from infected mothers during the third trimester, without adverse outcomes. One of these neonates had a positive SARS-CoV-2 PCR 36 hours after birth, leading to the suspicion of a perinatal transmission. Liu D. and colleagues (62) described briefly the outcomes of 13 newborns from infected mothers. Induced prematurity was noted in 54% (7/13), but none had neonatal complications. In the New-York series (42), which presented the outcomes of 18 infants from infected mothers, all but one had negative neonatal testing for SARS-CoV-2. One infant had an 'indeterminate' test result, which was clinically managed as a 'presumptive negative' diagnosis, as this result may reflect low level detection. In this series, 3 (3/18, 17%) instances of fetal distresses were noticed, one infant (1/18, 6%) was premature and one (1/18, 6%) presented with RDS with a concern for sepsis. Zeng and colleagues (63) reported the largest series to date, with 33 newborns included. A perinatal infection was suspected in three of them (3/33, 9%), with a positive PCR at day 2 and

4 of life. Infected newborns presented with higher rates of FGR, prematurity and complications at birth (fever, pneumonia, RDS, shortness of breath) than non-infected newborns: 33% vs 7%, 33% vs 10 %, 100% vs 10%, respectively. Wang (64) reported one case with a positive PCR in both the mother and her newborn (whereas placental and umbilical blood samples were negative). This newborn had lymphocytopenia, abnormal liver function and elevated creatine kinase, although was clinically stable. Congenital or perinatal transmission was also suspected in three other cases (65)(66). SARS-CoV-2 IgM antibodies were elevated in these three newborns, although their nasopharyngeal PCRs were negative. In an editorial related to these cases, Kimberlin (67) pointed out that false-positive results due to cross-reactivity of IgM could occur and perinatal testing remains a challenge.

Interestingly, Zamaniyan *and al.*(68), described a case of positive SARS-CoV-2 amniotic sample from a newborn, raising concern about potential vertical transmission in mothers with serious illness. Indeed, possible vertical transmission has been questioned by other authors (65,66) and remain unclear.

A case of second trimester miscarriage was reported by Baud *and al.*(69) in a patient at 19 WG positive for SARS-CoV-2. Virological findings confirmed the presence of the virus in the placenta, but not in fetal tissue or maternal samples, suggesting a potential impact of SARS-CoV-2 early in the pregnancy.

In other CoV infections during the second or third trimester of pregnancy, it is interesting to note that placental changes seem to precede FGR. Severe maternal respiratory illness related to CoV infection may lead to a circulatory insufficiency in both the placenta and the fetus. Thus,



a maternal COVID infection could affect the oxygen supply, leading to placental insufficiency, IUGR, fetal distress and / or fetal demise. A direct impact of the virus itself, by increasing fibrin deposits or thrombo-embolic events in the placenta, cannot be excluded and warrants further investigation.

Similarly, maternal SARS related to CoV-2 infection during the first trimester of pregnancy could disrupt the uterine placental flow, leading to miscarriage. Although the risk of miscarriage has been described with SARS-CoV-1 infection, no cases have yet been reported with SARS-CoV-2 infection.

## **MANAGEMENT OF PREGNANT WOMEN WITH A SEVERE ACUTE RESPIRATORY DISEASE**

Currently, no curative agent has been found for COVID-19. Studies conducted so far (including randomized controlled trials = RCTs) have been plagued by poor methods and reporting, such as exclusion of patients with worse outcome from the treated group, different endpoints between protocols and published reports, premature stopping of RCT (leading to lack of statistical power), use of endpoints of no clinical value (such as viral load), degrees of severity of enrolled patients (so that the benefit of a treatment or lack thereof in a cohort of patients may not generalizable to patients with different degrees of severity, lack of optimization of treatment dose or duration of treatment, to name but a few).

### **Pharmacological options for SARS-CoV-2 in pregnancy**

Several drugs are currently being evaluated as potential treatment for SARS-CoV-2 including hydroxychloroquine, lopinavir-ritonavir combination, remdesivir, oseltamivir, Interferon alpha, darunavir, baricitinib, tocilizumab and immunoglobulin therapy.

Hydroxychloroquine use in pregnant women has raised concerns in the past especially for an increased risk of cardiac malformation (70) and its retinal and ototoxicity (71)(72), related to the use of chloroquine and not hydroxychloroquine, findings which were not confirmed in more recent case series (73)(74)(75)(76). In the most recent systematic review and meta-analysis conducted in 2016, Kaplan YC et al (77), found no increase “in the rates of major congenital craniofacial and cardiovascular, nervous system and genitourinary malformations in the infants.” However, there was a significant increase in the spontaneous abortion rate, which could be associated with the underlying disease activity rather than the treatment. That being said, (hydroxy)chloroquine is one of the antimalarial drugs considered compatible with pregnancy in all trimesters for prophylaxis and treatment of malaria (78,79). A recent article gathered evidence on its use during lactation and found that it was compatible with breastfeeding (80), concluding that hydroxychloroquine could be used for the treatment of COVID-19 infection, in usual rheumatological doses (200-400 mg/day) if proven to be effective.

The lopinavir ritonavir combination is used as part of the HAART regimen to treat HIV infected women during pregnancy (81). In a systematic review that included 4,864 LPV/r-exposed pregnancies, the authors reported the rate of congenital abnormalities to be similar to that of the general population. However, the stillbirth rate was higher than in the general population in the UK (9.2 per 1000 infants against 4.7 per 1000 infants in 2013) (82). There has been general

concern regarding protease inhibitor exposure *in utero* and its association with an increased risk of preterm birth (83), however, to our knowledge this risk has not been evaluated specifically for lopinavir and ritonavir alone, and could be associated with the underlying disease activity rather than the treatment. Finally, moderate adverse events such as gastro-intestinal symptoms (84) and an increased risk for alteration in fasting glycemia (85) were reported. Lopinavir and ritonavir are drugs considered compatible with pregnancy in all trimesters for HIV treatment and has been associated with very low excretion into breastmilk (78,79).

Regarding remdesivir, no adverse effect was reported in pregnant participants in a randomized controlled trial on Ebola virus (86). Safety data on remdesivir in pregnancy are still scarce.

Oseltamivir was used during the 2009 influenza A/H1N1 pandemic and notably in pregnant mothers. In the most recent population-based study (87) conducted on 946,176 pregnancies in Denmark from 2002 to 2013 of which 1898 were exposed to oseltamivir during pregnancy, Ehrenstein.V and colleagues found no increased risk of any major congenital malformation, fetal death, preterm birth, SGA or low 5-min APGAR score. This confirmed previous observations from the European registry study (88) and the Roche Global Safety Database (89). Oseltamivir could be considered compatible with pregnancy in all trimesters if proven effective in COVID-19 treatment and has been associated with very low excretion into breastmilk (78,79).

The Interferon alpha drug (INF $\alpha$ ) is used to treat essential thrombocythemia, chronic myelocytic leukemia or hepatitis B and C in pregnant women. In a recent review including 43 exposed women, Sakai K *et al.* found that no adverse event had required discontinuation of the

treatment but alerted physicians to “pay attention to (...) rare adverse events, such as impaired liver function, interstitial pneumonia, and attempts at suicide” (90). Safety data on INF $\alpha$  in pregnancy are scarce but its similarity to beta interferon, of which safety data during pregnancy are substantial and reassuring, makes it compatible in pregnancy if proven effective for COVID-19 infection.

Regarding darunavir, no embryotoxicity or teratogenicity of this molecule was found in animal studies (91). In a brief review of darunavir use in pregnant women, the authors concluded that it is a well-tolerated molecule which has few minor adverse effects (92). Darunavir is considered compatible with pregnancy in all trimesters for HIV treatment despite its lack of safety data in pregnancy as its maternal benefit outweighs the potential unknown risks (78,79). Animal studies have demonstrated embryotoxicity of baricitinib (93) and no safety data are available in human.

Analysis of the Roche Global Safety Database does not suggest a substantially increased risk of malformations with the use of Tocilizumab. However, an increased rate of preterm birth and low birth weight children was possibly associated with TCZ exposure and could be associated with the underlying disease activity rather than the treatment (94). Safety data in pregnancy are limited and due to treatment-induced immunosuppression, an increased risk of maternal-fetal infections is theoretically possible in pregnant women treated with tocilizumab.

Finally, serum from convalescent COVID-19 patients and hyperimmune globulins specific to the novel coronavirus are currently being evaluated as therapeutic options (95).

Specific hyperimmune globulins have been used in several indications during pregnancy, including prevention of mother to child transmission of infectious diseases such as Hepatitis B

virus (HBV) (96) and Cytomegalovirus (CMV) (97), as well as convalescent serum recently in the Ebola virus disease (EBV) (98).

In a systematic review assessing the benefits and safety of hyperimmune globulins to prevent HBV mother to child transmission in 2440 pregnant women, only one study mentioned adverse events consisting in swelling in two women (96). More recently, convalescent serum to treat the Ebola virus disease was evaluated in a non randomized comparative study of 99 patients which included eight pregnant women. No serious adverse reaction were associated with the transfusion (98).

Two cases of pregnant women report the use of convalescent serum to treat SARS-CoV-2 infection (47,99). In the first case of a 31 years old pregnant woman, no serious adverse event related to the use of convalescent plasma was reported but its relative contribution to survival could not be determined due to other concomitant treatments. The authors concluded that its clinical benefit remained unknown (47). In the second case of a 35 year old pregnant woman with severe co morbidities who received both convalescent serum and remdesivir, no conclusion regarding safety or benefit of convalescent plasma could be drawn by the authors (99).

Data on the use of specific hyper immunoglobulins to prevent infections in pregnant women seem reassuring as well as those on the use of convalescent serum although they are more scarce. If they proved to be effective in COVID-19 treatment, convalescent serum and specific hyper immunoglobulins directed against SARS-CoV-2 could be considered compatible with pregnancy in all trimesters.

## **Prenatal monitoring** (Table 2)

Regarding potential asymptomatic infected pregnant women, the WHO recommends careful monitoring of patients with epidemiological history of contact with infected individuals, while *The American College of Obstetricians and Gynecologists* (ACOG) suggests routine antenatal care in this situation. An algorithm for assessment and management of symptomatic parturients has been proposed by ACOG, classifying them in three categories of risk: low, moderate and elevated. For mild presentations, women without comorbidities (low risk) should self-isolate at home, whereas those with health problems, obstetrical issues or the inability to care for themselves (moderate risk) should be seen in an ambulatory setting. According to *The Royal College of Obstetricians and Gynaecologists* (RCOG), pregnant women with moderate symptoms should self-isolate, unless they attend a maternity unit where patients in the 2<sup>nd</sup> or 3<sup>rd</sup> trimester meeting PHE criteria ( $\geq 1$  of: (1) Clinical/radiological evidence of pneumonia, (2) Acute Respiratory Distress Syndrome (ARDS), (3) Fever  $\geq 37.8$  and at least one of acute persistent cough, hoarseness, nasal discharge/congestion, shortness of breath, sore throat, wheezing or sneezing) should be tested for COVID-19 and treated as infected until results are available. When pregnant women present with severe symptoms (high risk), they should immediately go to an emergency department according to ACOG algorithm. All guidelines agree that administration of corticosteroids for fetal lung maturity is still recommended per protocol for in the setting of a high risk of preterm birth when the mother's condition is stable. Regarding fetal growth surveillance, RCOG recommends an antenatal ultrasound fourteen days after acute illness resolution for hospitalized patients, while ACOG suggests a 3<sup>rd</sup> trimester

ultrasound for COVID-19 pregnant women infected in 2<sup>nd</sup> and 3<sup>rd</sup> trimester. A detailed anatomy ultrasound could be considered for 1<sup>st</sup> trimester infections (ACOG).

### **Risk of thromboembolic disease**

Data suggest that COVID-19 may be associated with an increased thromboembolic risk with a rate of venous thromboembolism (VTE) of 39% in ICU patients (100). Therefore, routine VTE prophylaxis for hospitalized COVID-19 patients is recommended by the American Society of Hematology, the Society of Critical Care Medicine, and the International Society of Thrombosis and Haemostasis (101–103), in absence of contraindications. The decision between LMWH or unfractionated heparin (UFH) should be discussed with consideration for the risks and benefits. RCOG advises measures such as hydration and mobility for pregnant women isolated at home who are not taking thromboprophylaxis. If a woman has risk factors for VTE, a clinical review should be attempted and VTE risk assessed to consider the introduction of prophylactic treatment with LMWH at home. Routine thromboprophylaxis for hospitalized parturients with LMWH is suggested unless birth is expected within 12 hours. In the postpartum period, VTE risk should be assessed and the first dose of LMWH should be administered as soon as possible after birth. At the time of discharge from hospital, all women (antepartum or postpartum) should be prescribed at least 10 days of LMWH, according to RCOG recommendations. For management of critical illness, the WHO recommends the use of LMWH to reduce the incidence of VTE.

Use of prophylactic aspirin for the prevention of preeclampsia and other indications, such as antiphospholipid syndrome (APS) or prevention of fetal growth restriction, is controversial in

the context of COVID-19 infected women (104). Use of non-steroid anti-inflammatory drugs (NSAIDs) can worsen pulmonary disease and symptomatic COVID-19 non-pregnant patients treated with ibuprofen have experienced disease progression (105,106). However, ongoing RCT are evaluating the early use of aspirin in COVID-19 patients, which has the effects of inhibiting virus replication, anti-platelet aggregation, anti-inflammatory and anti-lung injury (107). For pregnant women, ACOG suggests decision on low-dose aspirin treatment should be taken individually. According to Kwiatkowski *and al.*(108), benefits of placental complications prevention outweigh the potential risks of adverse outcomes of SARS-CoV-2 infection related to low-dose aspirin prophylaxis.

## SUMMARY

For the first time in a century, we are facing a SARS-coronavirus global pandemic and we have to deal with numerous new challenges in terms of public health service. The global impact on pregnant women can only be hypothesized from recent observations gathered during the past few months from different parts of the world.

Other coronavirus epidemics, such as SARS-CoV-1 had a higher impact on pregnant women encompassing 40% of ICU admissions and 12% of mortalities. The MERS-CoV epidemic was even more lethal with a 40% mortality without significant difference of severity between pregnant and non-pregnant women. In this review, we gathered more than 150 cases of SARS-CoV-2 in pregnancy and identified a maternal mortality of 2.7% (9 cases) among those described in the literature. ICU admissions were between 6.9% and 8%. The proportion of



Accepted Article

severe complications seem to be equal to the non-pregnant population, however these must still be anticipated in pregnant women. These rates will have to be reviewed when the true denominator (number of infected pregnant women) is known, as a significant proportion of patients remain asymptomatic.

Past coronavirus epidemics were associated with adverse outcomes for the fetus and/or newborns including miscarriages (57%), preterm birth, fetal distress and FGR with SARS-CoV-1 infection during the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters. Also, MERS-CoV infection resulted in fetal and neonatal demise in 27% of cases. In this review, we found that of 142 cases of SARS-CoV-2 infections in pregnancy, 28% experienced preterm birth and 14% had adverse fetal/neonatal outcomes (FGR, fetal/neonatal demise, severe symptoms at birth). Potential mechanisms include placental changes, as observed with SARS-CoV-1, and severe respiratory maternal illness, which could lead to placental insufficiency, IUGR and fetal distress/demise. The role of SARS-CoV-2 in early adverse pregnancy outcomes needs further investigation.

With regards to pharmacological management, most agents currently tried are safe in pregnancy.

As of April 22, 2020, prenatal management should be adapted to the patient's condition as indicated by ACOG and other algorithms (109). There is currently no agreement on specific prenatal ultrasound surveillance, but due to the potential risk of IUGR, it would seem reasonable to assess fetal growth surveillance during the third trimester of pregnancy.

Administration of corticosteroids in pregnant women at risk of preterm birth should be administered per protocol, with consideration for the patient's condition. We recommend

considering parental preferences, the severity of illness and obstetrical indications when addressing the mode of delivery.

Guidelines for pregnancy management will continue to be updated and professionals should stay informed about new guidelines.

## **CONCLUSIONS AND FUTURE WORK**

The acquisition of robust data on the impact of emergent pathogens on pregnant women is often lacking or only available after a considerable delay (4) leaving scientists and clinicians to develop knowledge from intuition, extrapolation and case series as they emerge. Adaptive systems enabling prospective and structured collection of information on pregnant women during epidemics are needed. They allow for faster knowledge acquisition, through specific epidemiological studies based on robust data, and tailoring of preventive and screening strategies to improve maternal, fetal and neonatal outcomes in a timely manner. Recruitment of pregnant women with COVID-19 in cohort studies should be encouraged globally to allow for evidence-based management. Currently, several registries are open for recruitment. COVI-Preg is an international hospital-based registry enrolling pregnant women at any stage of pregnancy with a suspected SARS-CoV-2 infection (110). PRIORITY (Pregnancy CoRonavIrus Outcomes RegIsTrY) is a US nationwide study of pregnant or postpartum women who are either under investigation for Coronavirus infection (COVID-19) or have been confirmed to have COVID-19 (111). CHOPAN (Coronavirus Health Outcomes in Pregnancy and Neonates) is a hospital-based registry aiming to collect real-time data on pregnant women who are infected with SARS-CoV2 in Australia, New Zealand & the Pacific region (112). International Registry

of Coronavirus (COVID-19) Exposure in Pregnancy (IRCEP) is a patient-based registry enrolling any women who are currently pregnant or have been pregnant within the last 6 months, and who have been tested for SARS-CoV-2 (regardless of the result) or have been clinically diagnosed with COVID-19 by a health care professional (113).

These initiatives should provide several datasets available for research aiming to improve pregnant patient care during the COVID-19 pandemic in the near future.

## REFERENCES

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020 Feb;395(10223):497–506.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine*. 2020 Feb 20;382(8):727–33.
3. Siston AM, Rasmussen SA, Honein MA, Fry AM, Seib K, Callaghan WM, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA*. 2010 Apr 21;303(15):1517–25.
4. Musso D, Ko AI, Baud D. Zika Virus Infection - After the Pandemic. *N Engl J Med*. 2019 10;381(15):1444–57.
5. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol*. 2016;14(8):523–34.
6. van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *New England Journal of Medicine*. 2020 Apr 16;382(16):1564–7.
7. Hunter E, Price DA, Murphy E, Loeff IS van der, Baker KF, Lendrem D, et al. First experience of COVID-19 screening of health-care workers in England. *The Lancet* [Internet]. 2020 Apr 22 [cited 2020 Apr 27];0(0). Available from: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30970-3/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30970-3/abstract)
8. WHO | Summary table of SARS cases by country, 1 November 2002 - 7 August 2003

[Internet]. WHO. World Health Organization; [cited 2020 Apr 24]. Available from:  
[https://www.who.int/csr/sars/country/2003\\_08\\_15/en/](https://www.who.int/csr/sars/country/2003_08_15/en/)

9. WHO | Middle East respiratory syndrome coronavirus (MERS-CoV) [Internet]. WHO. World Health Organization; [cited 2020 Apr 24]. Available from:  
<http://www.who.int/emergencies/mers-cov/en/>

10. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. *New England Journal of Medicine*. 2020 Mar 26;382(13):1199–207.

11. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. 2020 Apr 7;323(13):1239–42.

12. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* [Internet]. 2020 Apr 22 [cited 2020 Apr 27]; Available from:  
<https://jamanetwork.com/journals/jama/fullarticle/2765184>

13. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020 Feb 7;

14. Middeldorp S, Coppens M, Haaps TF van, Foppen M, Vlaar AP, Muller MCA, et al. Incidence of Venous Thromboembolism in Hospitalized Patients with COVID-19. 2020 Apr 19 [cited 2020 Apr 22]; Available from:

<https://www.preprints.org/manuscript/202004.0345/v1>

15. Rasmussen SA, Smulian JC, Lednický JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. *American Journal of Obstetrics and Gynecology* [Internet]. 2020 Feb [cited 2020 Apr 6]; Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0002937820301976>
16. Alberti P, Beretta S, Piatti M, Karantzoulis A, Piatti ML, Santoro P, et al. Guillain-Barré syndrome related to COVID-19 infection. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(4).
17. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA*. 2020 Apr 14;323(14):1406–7.
18. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet*. 2020 Feb 15;395(10223):514–23.
19. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis*. 2020 Mar 12;
20. Baud D, Nielsen-Saines K, Qi X, Musso D, Pomar L, Favre G. Authors' reply. *The Lancet Infectious Diseases*. 2020 Mar;S1473309920302553.
21. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *The Lancet Infectious Diseases* [Internet]. 2020 Mar 30 [cited 2020 Apr 27];0(0). Available from: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30243-7/abstract](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/abstract)
22. Callaghan WM, Creanga AA, Jamieson DJ. Pregnancy-Related Mortality Resulting

From Influenza in the United States During the 2009–2010 Pandemic: Obstetrics & Gynecology. 2015 Sep;126(3):486–90.

23. Favre G, Pomar L, Musso D, Baud D. 2019-nCoV epidemic: what about pregnancies? *The Lancet*. 2020 Feb;395(10224):e40.

24. Zhang J, Wang Y, Chen L, Zhang R, Xie Y. [Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome]. *Zhonghua Fu Chan Ke Za Zhi*. 2003 Aug;38(8):516–20.

25. Shek CC, Ng PC, Fung GPG, Cheng FWT, Chan PKS, Peiris MJS, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatrics*. 2003 Oct;112(4):e254.

26. Lau K-K, Yu W-C, Chu C-M, Lau S-T, Sheng B, Yuen K-Y. Possible central nervous system infection by SARS coronavirus. *Emerging Infect Dis*. 2004 Feb;10(2):342–4.

27. Robertson CA, Lowther SA, Birch T, Tan C, Sorhage F, Stockman L, et al. SARS and pregnancy: a case report. *Emerging Infect Dis*. 2004 Feb;10(2):345–8.

28. Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Wong TY, et al. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *BJOG*. 2004 Aug;111(8):771–4.

29. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol*. 2004 Jul;191(1):292–7.

30. Yudin MH, Steele DM, Sgro MD, Read SE, Kopplin P, Gough KA. Severe acute respiratory syndrome in pregnancy. *Obstet Gynecol*. 2005 Jan;105(1):124–7.

31. Payne DC, Iblan I, Alqasrawi S, Al Nsour M, Rha B, Tohme RA, et al. Stillbirth

during infection with Middle East respiratory syndrome coronavirus. *J Infect Dis.* 2014 Jun 15;209(12):1870–2.

32. Racelis S, de los Reyes VC, Sucaldito MN, Deveraturda I, Roca JB, Tayag E. Contact tracing the first Middle East respiratory syndrome case in the Philippines, February 2015. *Western Pac Surveill Response J.* 2015 Jun 27;6(3):3–7.

33. Shek CC, Ng PC, Fung GPG, Cheng FWT, Chan PKS, Peiris MJS, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatrics.* 2003 Oct;112(4):e254.

34. Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC Infect Dis.* 2016 Mar 2;16:105.

35. Assiri A, Abedi GR, Al Masri M, Saeed AB, Gerber SI, Watson JT. Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases From Saudi Arabia. *Clin Infect Dis.* 2016 Oct 1;63(7):951–3.

36. Jeong SY, Sung SI, Sung JH, Ahn SY, Kang ES, Chang YS, et al. MERS-CoV Infection in a Pregnant Woman in Korea. *J Korean Med Sci.* 2017 Oct;32(10):1717–20.

37. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *Journal of Microbiology, Immunology and Infection.* 2019 Jun 1;52(3):501–3.

38. Malik A, El Masry KM, Ravi M, Sayed F. Middle East Respiratory Syndrome Coronavirus during Pregnancy, Abu Dhabi, United Arab Emirates, 2013. *Emerging Infect Dis.* 2016 Mar;22(3):515–7.

39. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, et al. Clinical Characteristics of



Pregnant Women with Covid-19 in Wuhan, China. *New England Journal of Medicine*. 2020 Apr 17;0(0):null.

40. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases. *Am J Obstet Gynecol*. 2020 Apr 23;

41. Ferrazzi EM, Frigerio L, Cetin I, Vergani P, Spinillo A, Prefumo F, et al. COVID-19 Obstetrics Task Force, Lombardy, Italy: executive management summary and short report of outcome. *International Journal of Gynecology & Obstetrics* [Internet]. [cited 2020 Apr 15];n/a(n/a). Available from:

<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.13162>

42. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM* [Internet]. 2020 Apr 9 [cited 2020 Apr 13]; Available from:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144599/>

43. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM*. 2020 Apr 9;100118.

44. Karami P, Naghavi M, Feyzi A, Aghamohammadi M, Novin MS, Mobaien A, et al. Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings. *Travel Med Infect Dis*. 2020 Apr 10;101665.

45. Zamaniyan M, Ebadi A, Aghajanpoor Mir S, Rahmani Z, Haghshenas M, Azizi S.

Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. *Prenat Diagn.* 2020 Apr 17;

46. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal Death Due to COVID-19 Disease. *American Journal of Obstetrics & Gynecology* [Internet]. 2020 Apr 28 [cited 2020 May 3];0(0). Available from: [https://www.ajog.org/article/S0002-9378\(20\)30516-0/abstract](https://www.ajog.org/article/S0002-9378(20)30516-0/abstract)

47. Zhang B, Liu S, Tan T, Huang W, Dong Y, Chen L, et al. Treatment with convalescent plasma for critically ill patients with SARS-CoV-2 infection. *Chest.* 2020 Mar 31;

48. Juusela A, Nazir M, Gimovsky M. Two Cases of COVID-19 Related Cardiomyopathy in Pregnancy. *American Journal of Obstetrics & Gynecology MFM.* 2020 Apr 3;100113.

49. Favre G, Pomar L, Baud D. COVID-19 during pregnancy: Do not underestimate the risk of maternal adverse outcomes.

50. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *American Journal of Obstetrics and Gynecology.* 2004 Jul;191(1):292–7.

51. Ng WF, Wong SF, Lam A, Mak YF, Yao H, Lee KC, et al. The placentas of patients with severe acute respiratory syndrome: a pathophysiological evaluation. *Pathology.* 2006 Jun;38(3):210–8.

52. Zhang J, Wang Y, Chen L, Zhang R, Xie Y. [Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome]. *Zhonghua Fu Chan Ke Za Zhi.* 2003 Aug;38(8):516–20.

53. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *Journal of Microbiology, Immunology and Infection*. 2019 Jun;52(3):501–3.
54. Alfaraj SH, Al-Tawfiq JA, Altuwaijri TA, Memish ZA. Middle East respiratory syndrome coronavirus in pediatrics: a report of seven cases from Saudi Arabia. *Front Med*. 2019 Feb 1;13(1):126–30.
55. Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, Watson JT. Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases From Saudi Arabia. *Clin Infect Dis*. 2016 Oct 1;63(7):951–3.
56. Payne DC, Iblan I, Alqasrawi S, Al Nsour M, Rha B, Tohme RA, et al. Stillbirth During Infection With Middle East Respiratory Syndrome Coronavirus. *J Infect Dis*. 2014 Jun 15;209(12):1870–2.
57. Jeong SY, Sung SI, Sung J-H, Ahn SY, Kang E-S, Chang YS, et al. MERS-CoV Infection in a Pregnant Woman in Korea. *Journal of Korean Medical Science*. 2017 Oct 1;32(10):1717–20.
58. Li N, Han L, Peng M, Lv Y, Ouyang Y, Liu K, et al. Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study. *Clin Infect Dis* [Internet]. [cited 2020 Apr 13]; Available from: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa352/5813589>
59. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Translational Pediatrics*. 2020 Feb;9(1):51–60.

60. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *Journal of Infection* [Internet]. 2020 Mar [cited 2020 Apr 6]; Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0163445320301092>
61. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet*. 2020 Mar;395(10226):809–15.
62. Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. *American Journal of Roentgenology*. 2020 Mar 18;1–6.
63. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr* [Internet]. 2020 Mar 26 [cited 2020 Apr 13]; Available from: <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2763787>
64. Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A Case Report of Neonatal 2019 Coronavirus Disease in China. *Clin Infect Dis* [Internet]. [cited 2020 Apr 17]; Available from: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa225/5803274>
65. Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in Infants Born to Mothers With COVID-19 Pneumonia. *JAMA* [Internet]. 2020 Mar 26 [cited 2020 Apr 17]; Available from: <https://jamanetwork.com/journals/jama/fullarticle/2763854>
66. Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *JAMA* [Internet]. 2020 Mar 26 [cited 2020 Apr 17]; Available from:

<https://jamanetwork.com/journals/jama/fullarticle/2763853>

67. Kimberlin DW, Stagno S. Can SARS-CoV-2 Infection Be Acquired In Utero?: More Definitive Evidence Is Needed. JAMA [Internet]. 2020 Mar 26 [cited 2020 Apr 17];

Available from: <https://jamanetwork.com/journals/jama/fullarticle/2763851>

68. Zamaniyan M, Ebadi A, Mir SA, Rahmani Z, Haghshenas M, Azizi S. Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission. Prenatal Diagnosis [Internet]. [cited 2020 Apr 20];n/a(n/a). Available from:

<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/pd.5713>

69. Baud D, Greub G, Favre G, Gengler C, Jaton K, Dubruc E, et al. Second-Trimester Miscarriage in a Pregnant Woman With SARS-CoV-2 Infection. JAMA [Internet]. 2020 Apr 30 [cited 2020 May 3]; Available from:

<https://jamanetwork.com/journals/jama/fullarticle/2765616>

70. Klinger G, Morad Y, Westall CA, Laskin C, Spitzer KA, Koren G, et al. Ocular toxicity and antenatal exposure to chloroquine or hydroxychloroquine for rheumatic diseases. The Lancet. 2001 Sep 8;358(9284):813–4.

71. Jr L. Profound childhood deafness. Inner ear pathology. Ann Otol Rhinol Laryngol. 1973 Mar 1;82:Suppl 5:1-121.

72. Matz GJ, Naunton RF. Ototoxicity of Chloroquine. Arch Otolaryngol. 1968 Oct 1;88(4):370–2.

73. Levy RA, Vilela VS, Cataldo MJ, Ramos RC, Duarte JL, Tura BR, et al. Hydroxychloroquine (HCQ) in lupus pregnancy: double-blind and placebo-controlled study. Lupus. 2001 Jun 1;10(6):401–4.

74. Costedoat-Chalumeau N, Amoura Z, Duhaut P, Huong DLT, Sebbough D, Wechsler B, et al. Safety of hydroxychloroquine in pregnant patients with connective tissue diseases: A study of one hundred thirty-three cases compared with a control group. *Arthritis & Rheumatism*. 2003;48(11):3207–11.
75. Cimaz R, Brucato A, Meregalli E, Muscará M, Sergi P. Electoretinograms of children born to mothers treated with hydroxychloroquine during pregnancy and breast-feeding: Comment on the article by Costedoat-Chalumeau et al. *Arthritis & Rheumatism*. 2004;50(9):3056–7.
76. Motta M, Tincani A, Faden D, Zinzini E, Lojacono A, Marchesi A, et al. Follow-Up of Infants Exposed to Hydroxychloroquine Given to Mothers during Pregnancy and Lactation. *Journal of Perinatology*. 2005 Feb;25(2):86–9.
77. Kaplan Y, Koren G. Use of hydroxychloroquine during pregnancy and breastfeeding: An update for the recent coronavirus pandemic (COVID-19). 2020 Mar 29;
78. Briggs G. *Drugs in Pregnancy and Lactation* [Internet]. [cited 2020 May 3]. Available from: <https://shop.lww.com/Drugs-in-Pregnancy-and-Lactation/p/9781496349620>
79. Schaefer Christof. *Drugs During Pregnancy and Lactation - 3rd Edition* [Internet]. [cited 2020 May 3]. Available from: <https://www.elsevier.com/books/drugs-during-pregnancy-and-lactation/schaefer/978-0-12-408078-2>
80. Chu CM, Cheng VCC, Hung IFN, Wong MML, Chan KH, Chan KS, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*. 2004 Mar 1;59(3):252–6.
81. Pasley MV, Martinez M, Hermes A, d'Amico R, Nilus A. Safety and efficacy of

lopinavir/ritonavir during pregnancy: a systematic review. *AIDS Rev.* 2013 Mar;15(1):38–48.

82. Tookey PA, Thorne C, van Wyk J, Norton M. Maternal and foetal outcomes among 4118 women with HIV infection treated with lopinavir/ritonavir during pregnancy: analysis of population-based surveillance data from the national study of HIV in pregnancy and childhood in the United Kingdom and Ireland. *BMC Infectious Diseases.* 2016 Feb 4;16(1):65.

83. Zash R, Jacobson DL, Diseko M, Mayondi G, Mmalane M, Essex M, et al. Comparative Safety of Antiretroviral Treatment Regimens in Pregnancy. *JAMA Pediatr.* 2017 02;171(10):e172222.

84. Brites C, Nóbrega I, Luz E, Travassos AG, Lorenzo C, Netto EM. Raltegravir versus lopinavir/ritonavir for treatment of HIV-infected late-presenting pregnant women. *HIV Clin Trials.* 2018;19(3):94–100.

85. Delicio AM, Lajos GJ, Amaral E, Lopes F, Cavichioli F, Myoshi I, et al. Adverse effects of antiretroviral therapy in pregnant women infected with HIV in Brazil from 2000 to 2015: a cohort study. *BMC Infect Dis [Internet].* 2018 Sep 27 [cited 2020 Apr 10];18.

Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6161436/>

86. Mulangu S, Dodd LE, Davey RT, Tshiani Mbaya O, Proschan M, Mukadi D, et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *New England Journal of Medicine.* 2019 Dec 12;381(24):2293–303.

87. Ehrenstein V, Kristensen NR, Monz BU, Clinch B, Kenwright A, Sørensen HT. Oseltamivir in pregnancy and birth outcomes. *BMC Infect Dis.* 2018 Oct 16;18(1):519.

88. Graner S, Svensson T, Beau A-B, Damase-Michel C, Engeland A, Furu K, et al.

Neuraminidase inhibitors during pregnancy and risk of adverse neonatal outcomes and congenital malformations: population based European register study. *BMJ* [Internet]. 2017 Feb 28 [cited 2020 Apr 10];356. Available from: <https://www.bmj.com/content/356/bmj.j629>

89. Wollenhaupt M, Chandrasekaran A, Tomianovic D. The safety of oseltamivir in pregnancy: an updated review of post-marketing data. *Pharmacoepidemiol Drug Saf.* 2014 Oct;23(10):1035–42.

90. Sakai K, Ueda A, Hasegawa M, Ueda Y. Efficacy and safety of interferon alpha for essential thrombocythemia during pregnancy: two cases and a literature review. *Int J Hematol.* 2018 Aug;108(2):203–7.

91. Federal Drug Administration. PREZISTA (darunavir) Label. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/021976s045\\_202895s020lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021976s045_202895s020lbl.pdf).

92. Pope R, Kashuba A. Darunavir for use in pregnant women with HIV. *Expert Rev Clin Pharmacol.* 2017 Dec;10(12):1317–27.

93. Winthrop KL. The emerging safety profile of JAK inhibitors in rheumatic disease. *Nat Rev Rheumatol.* 2017;13(5):320.

94. Hoeltzenbein M, Beck E, Rajwanshi R, Gøtestam Skorpen C, Berber E, Schaefer C, et al. Tocilizumab use in pregnancy: Analysis of a global safety database including data from clinical trials and post-marketing data. *Semin Arthritis Rheum.* 2016;46(2):238–45.

95. Valk SJ, Piechotta V, Chai KL, Doree C, Monsef I, Wood EM, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a rapid review. *Cochrane Database Syst Rev.* 2020 14;5:CD013600.

96. Chen Z, Zeng M, Liu D, Wu L, Zhang L. Antenatal administration of hepatitis B



immunoglobulin and hepatitis B vaccine to prevent mother to child transmission in hepatitis B virus surface antigen positive pregnant women: A systematic review and meta-analysis.

Medicine (Baltimore). 2020 Apr;99(16):e19886.

97. Minsart A-F, Smiljkovic M, Renaud C, Gagné M-P, Lamarre V, Kakkar F, et al. Use of Cytomegalovirus-Specific Hyperimmunoglobulins in Pregnancy: A Retrospective Cohort. *J Obstet Gynaecol Can.* 2018;40(11):1409–16.

98. van Griensven J, Edwards T, de Lamballerie X, Semple MG, Gallian P, Baize S, et al. Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea. *New England Journal of Medicine.* 2016 Jan 7;374(1):33–42.

99. Anderson J, Schauer J, Bryant S, Graves CR. The use of convalescent plasma therapy and remdesivir in the successful management of a critically ill obstetric patient with novel coronavirus 2019 infection: A case report. *Case Rep Womens Health [Internet].* 2020 May 16 [cited 2020 May 22]; Available from:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7229947/>

100. Middeldorp S, Coppens M, Haaps TF van, Foppen M, Vlaar AP, Muller MCA, et al. Incidence of Venous Thromboembolism in Hospitalized Patients with COVID-19. 2020 Apr 19 [cited 2020 May 3]; Available from:

<https://www.preprints.org/manuscript/202004.0345/v1>

101. Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *Journal of Thrombosis and Haemostasis.* 2020;18(5):1023–6.

102. COVID-19 and VTE-Anticoagulation - Hematology.org [Internet]. [cited 2020 Apr

30]. Available from: <https://www.hematology.org:443/covid-19/covid-19-and-vte-anticoagulation>

103. SCCM | COVID-19 Guidelines [Internet]. Society of Critical Care Medicine (SCCM). [cited 2020 Apr 30]. Available from:

<https://sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19>

104. Mathilde G, Rolnik DL, Hoffman MK, Panchaud A, Baud D. Should we stop aspirin prophylaxis in pregnant women diagnosed with COVID-19? *Ultrasound in Obstetrics & Gynecology* [Internet]. [cited 2020 May 3];n/a(n/a). Available from:

<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.22063>

105. Day M. Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists. *BMJ* [Internet]. 2020 Mar 17 [cited 2020 May 12];368. Available from:

<https://www.bmj.com/content/368/bmj.m1086>

106. Voiriot G, Chalumeau M, Messika J, Basille D, Philippe B, Ricard J-D, et al. [Risks associated with the use of non-steroidal anti-inflammatory drugs during pneumonia]. *Rev Mal Respir.* 2018 Apr;35(4):430–40.

107. Protective Effect of Aspirin on COVID-19 Patients - Full Text View -

*ClinicalTrials.gov* [Internet]. [cited 2020 May 12]. Available from:

<https://clinicaltrials.gov/ct2/show/NCT04365309>

108. Kwiatkowski S, Borowski D, Kajdy A, Poon LC, Rokita W, Wielgoś M. Why we should not stop giving aspirin to pregnant women during the COVID-19 pandemic.

*Ultrasound in Obstetrics & Gynecology* [Internet]. [cited 2020 May 11];n/a(n/a). Available from: <https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.22049>

## TABLES

**Table 1:** Fetal and neonatal outcomes after coronavirus infection during pregnancy.

*FGR, Fetal growth restriction; RDS, respiratory distress syndrome*

*\* missing data in the description of fetal / neonatal outcomes*

**Table 2 :** Comparison of different recommendations for management of COVID-19 pregnant women. *WHO, World Health Organization ; ACOG, The American College of Obstetricians and Gynecologists ; RCOG, Royal College of Obstetricians & Gynaecologists ; RCPCH, Royal College of Paediatrics and Child Health.*

## FIGURES

**Figure 1 :** Timeline of main events, total number of confirmed cases by WHO and total number confirmed deaths by WHO from December 2019.

**Figure 2 :** Number of publication for SARS-CoV-2 from December 2019, compared to HIV (1983-1986) and Zika virus (2016).

**Figure 3 :** Flowchart describing the process of article selection and the number of articles.

## ANNEXE

**Annexe 1 :** Publications for: “(COVID-19 OR SARS-Cov2 OR coronavirus) and (pregnancy OR pregnant)” research on PubMed on 22 April 2020.

**Table 1: Fetal and neonatal outcomes after coronavirus infection during pregnancy**

	MERS-CoV	SARS-CoV 1			SARS-CoV 2												
	Alfaraj, 2019	Wong, 2004	Zhang, 2003	TOTAL	Zhu, 2020	Li, 2020	Breslin, 2020	Yu, 2020	Liu D., 2020	Chen, 2020	Zeng, 2020	Liu Y., 2020	Zhang, 2020	Yin, 2020	Yang, 2020	Case reports	TOTAL
1st Trimester infection	n=1	n=7	n=0	n=7	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=0	n=4	n=0	n=0	n=4
-TOP		2 (29%)		2 (29%)										3 (75%)			3 (75%)
-miscarriages	0 (0%)	4 (57%)		4 (57%)										0 (0%)			0 (0%)
2nd and 3rd Trimester infection	n=10	n=5	n=5	n=10	n=10	n=17	n=18	n=7	n=13	n=9	n=33	n=10	n=16	n=17	n=13	n=11	n=174
-FGR	*	2 (40%)	*	2/5 * (40%)	2 (20%)	3 (18%)	*	0 (0%)	*	2 (22%)	3 (9%)	*	*	1 (6%)	*	1 (9%)	12/102 * (12%)
-fetal distress	*	1 (20%)	*	1/5 * (20%)	6 (60%)	2 (12%)	3 (17%)	*	*	2 (22%)	*	*	*	1 (6%)	*	3 (27%)	21/141 * (15%)
-fetal demise	2 (20%)	0 (0%)	1 (20%)	1/10 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	1/174 (1%)
-preterm birth <37w	5 (50%)	2 (40%)	*	2/5 * (40%)	6 (60%)	4 (24%)	1 (6%)	0 (0%)	7 (54%)	4 (44%)	4 (12%)	6 (60%)	3 (19%)	5 (29%)	2 (15%)	7 (64%)	49/174 (28%)
-neonatal demise	1 (10%)	0 (0%)	*	0/5 * (0%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	2/173 (1%)
-RDS at birth	*	2 (40%)	*	2/5 * (40%)	6 (60%)	0 (0%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	4 (12%)	0 (0%)	1 (6%)	0 (0%)	3 (23%)	2 (18%)	14/173 (8%)
-other complications	*	2 (40%)	*	2/5 * (40%)	6 (60%)	1 (6%)	0 (0%)	0 (0%)	*	0 (0%)	4 (12%)	0 (0%)	1 (6%)	0 (0%)	*	4 (36%)	16/147 * (11%)
Suspected perinatal Infection	*	0 (0%)	*	0/5 * (0%)	0/9 * (0%)	0 (0%)	1 (6%)	1/3 * (33%)	*	0/6 * (0%)	3 (9%)	0 (0%)	0/10 * (0%)	0 (0%)	0 (0%)	2/10 * (20%)	7/146 * (5%)

MERS : (1–3)  
 SARS-CoV-1 : (4,5)  
 SARS-CoV-2 : (6–15)  
 Case-reports of SARS-CoV2 infections during pregnancy includes: (16–21)

**Abbreviations:** FGR, Fetal growth restriction; RDS, respiratory distress syndrome  
 Missing data in the description of fetal / neonatal outcomes

**References**

- Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *Journal of Microbiology, Immunology and Infection*. 2019 Jun;52(3):501–3.
- Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, Watson JT. Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases From Saudi Arabia. *Clin Infect Dis*. 2016 Oct 1;63(7):951–3.
- Payne DC, Iblan I, Alqasrawi S, Al Nsour M, Rha B, Tohme RA, et al. Stillbirth During Infection With Middle East Respiratory Syndrome Coronavirus. *J Infect Dis*. 2014 Jun 15;209(12):1870–2.
- Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *American Journal of Obstetrics and Gynecology*. 2004 Jul;191(1):292–7.
- Zhang J, Wang Y, Chen L, Zhang R, Xie Y. [Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome]. *Zhonghua Fu Chan Ke Za Zhi*. 2003 Aug;38(8):516–20.
- Li N, Han L, Peng M, Lv Y, Ouyang Y, Liu K, et al. Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2020 Mar [cited 2020 Apr 7]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2020.03.10.20033605>
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet*. 2020 Mar;395(10226):809–15.
- Yu N, Li W, Kang Q, Xiong Z, Wang S, Lin X, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *The Lancet Infectious Diseases*. 2020 Mar;S1473309920301766.
- Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Translational Pediatrics*. 2020 Feb;9(1):51–60.
- Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. *American Journal of Roentgenology*. 2020 Mar 18;1–6.
- Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr* [Internet]. 2020 Mar 26 [cited 2020 Apr 13]; Available from: <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2763787>
- Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *Journal of Infection* [Internet]. 2020 Mar [cited 2020 Apr 6]; Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0163445320301092>
- Zhang L, Jiang Y, Wei M, Cheng BH, Zhou XC, Li J, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. *Zhonghua Fu Chan Ke Za Zhi*. 2020 Mar 7;55(0):E009.
- yang H, Sun G, Tang F, Peng M, Gao Y, Peng J, et al. Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019. *J Infect* [Internet]. 2020 Apr 12 [cited 2020 Apr 21]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7152867/>
- Chen Y, Peng H, Wang L, Zhao Y, Zeng L, Gao H, et al. Infants Born to Mothers With a New Coronavirus (COVID-19). *Front Pediatr* [Internet]. 2020 Mar 16 [cited 2020 Apr 22];8. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7098456/>
- Fan C, Lei D, Fang C, Li C, Wang M, Liu Y, et al. Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry? *Clin Infect Dis*. 2020 Mar 17;
- Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis*. 2020 Mar 12;
- Wang X, Zhou Z, Zhang J, Zhu F, Tang Y, Shen X. A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. *Clinical Infectious Diseases* [Internet]. 2020 Feb 28 [cited 2020 Apr 6]; Available from: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa200/5771323>
- Gidlof S, Savchenko J, Brune T, Josefsson H. COVID-19 in pregnancy with comorbidities: More liberal testing strategy is needed. *Acta Obstet Gynecol Scand*. 2020 Apr 6;
- Iqbal SN, Overcash R, Mokhtari N, Saeed H, Gold S, Auguste T, et al. An Uncomplicated Delivery in a Patient with Covid-19 in the United States. *N Engl J Med*. 2020 16;382(16):e34.
- Lee DH, Lee J, Kim E, Woo K, Park HY, An J. Emergency cesarean section on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) confirmed patient. *Korean J Anesthesiol*. 2020 Mar 31;

	WHO <sup>1</sup>	ACOG <sup>2</sup>	RCOG <sup>3</sup>	RCPCH <sup>4</sup>
<b>Pregnant women with history of SARS-CoV-2 exposure</b>	Monitor carefully	If asymptomatic, routine prenatal care	-	-
<b>Mild/Moderate symptoms, suspected or confirmed COVID-19 pregnant women</b>	Woman-centered, respectful skilled care, including obstetric, fetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications	In presence of comorbidities, obstetric issues or inability to care for self, see patient in ambulatory setting. If not, self-isolation is recommended. Pregnant women should be prioritized for COVID-19 testing	Self-isolation at home. If attending a maternity unit and meet PHE criteria <sup>5</sup> , pregnant women in 2 <sup>nd</sup> or 3 <sup>rd</sup> trimester should be tested. Should be treated as infected until results are available	-
<b>Moderate/Severe symptoms, COVID-19 positive women</b>		In case of severe symptoms (ACOG algorithm <sup>6</sup> ), admission to emergency unit in isolation. Fetal management as any ill pregnant women	Hourly monitored (oxygen Sat >94%). Prophylactic LMWH (unless birth expected within 12 hours). Chest CT if indicated. Assess if caesarean birth or labour induction is indicated	-
<b>Fetal monitoring for COVID-19 positive mothers</b>	-	1 <sup>st</sup> trimester infection: Detailed anatomy ultrasound could be considered. 2 <sup>nd</sup> -3 <sup>rd</sup> trimester infection: fetal growth ultrasound in 3 <sup>rd</sup> trimester.	Refer to antenatal ultrasound for fetal growth surveillance 14 days after resolution of acute illness for patients who have been hospitalized only.	
<b>Corticosteroid administration for fetal benefit (when risk of preterm birth)</b>	For mildly symptomatic mothers when fetal benefits outweigh potential harm to the mother.	Recommended between 24 0/7 weeks and 33 6/7 weeks of gestation. Not routinely recommended in late preterm period	Indicated as in NICE guidance <sup>7</sup> .	Indicated as normal practice.

- General guidance for healthcare staff: using appropriate PPE. (WHO, ACOG, RCOG)

**Table 2. Comparison of different recommendations for management of COVID-19 pregnant women.**

---

<sup>1</sup> Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance V 1.2. *WHO. 13 March 2020. Last update 29 April.*

<sup>2</sup> Novel Coronavirus 2019 (COVID-19), Practice Advisory. *The American College of Obstetricians and Gynecologists. 13 March 2020. Last update 23 April.*

<sup>3</sup> Coronavirus (COVID-19) Infection in Pregnancy, Information for healthcare professionals Version 7. *Royal College of Obstetricians & Gynaecologists. 17 April 2020.*

<sup>4</sup> COVID-19 - guidance for neonatal settings. *Royal College of Paediatrics and Child Health. 14 April 2020.*

<sup>5</sup> Current criteria PHE criteria (correct at the time of publishing this update) are: Women who are being/are admitted to hospital with one of the following:

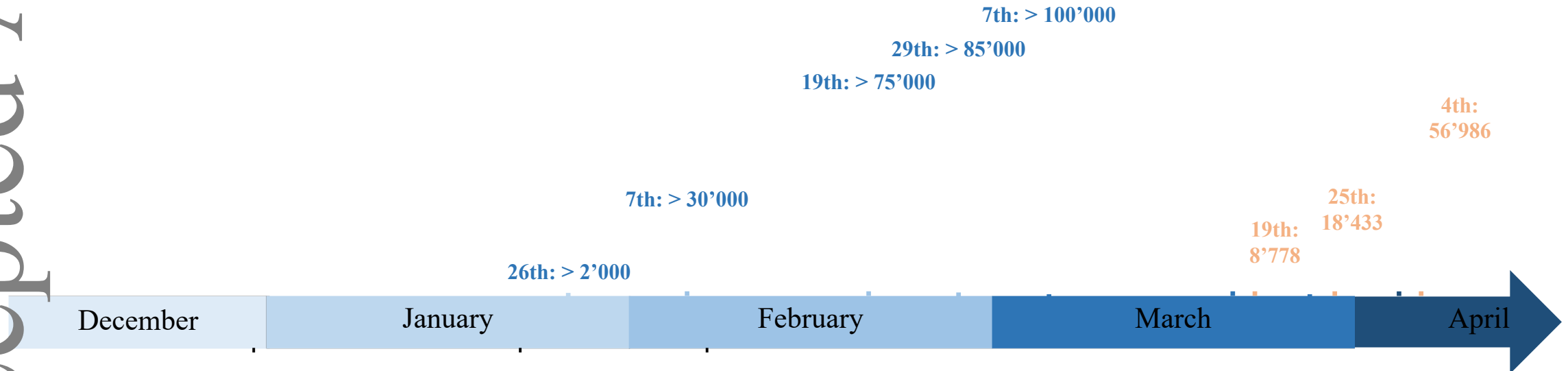
- Clinical/radiological evidence of pneumonia,
- Acute Respiratory Distress Syndrome (ARDS),
- Fever  $\geq 37.8$  AND at least one of acute persistent cough, hoarseness, nasal discharge/congestion, shortness of breath, sore throat, wheezing or sneezing.

<sup>6</sup> ACOG algorithm available at : <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019>

<sup>7</sup> Preterm labour and birth, NICE guideline (NG25), published 20 November 2015, updated 02 August 2019. *National Institute for Health and Care Excellence. Available at:*

<https://www.nice.org.uk/guidance/ng25/chapter/recommendations#maternal-corticosteroids>

Number of confirmed cases  
 Number of deaths



December 31st: First reported case in Wuhan.

January 7th: A novel coronavirus is identified in China.

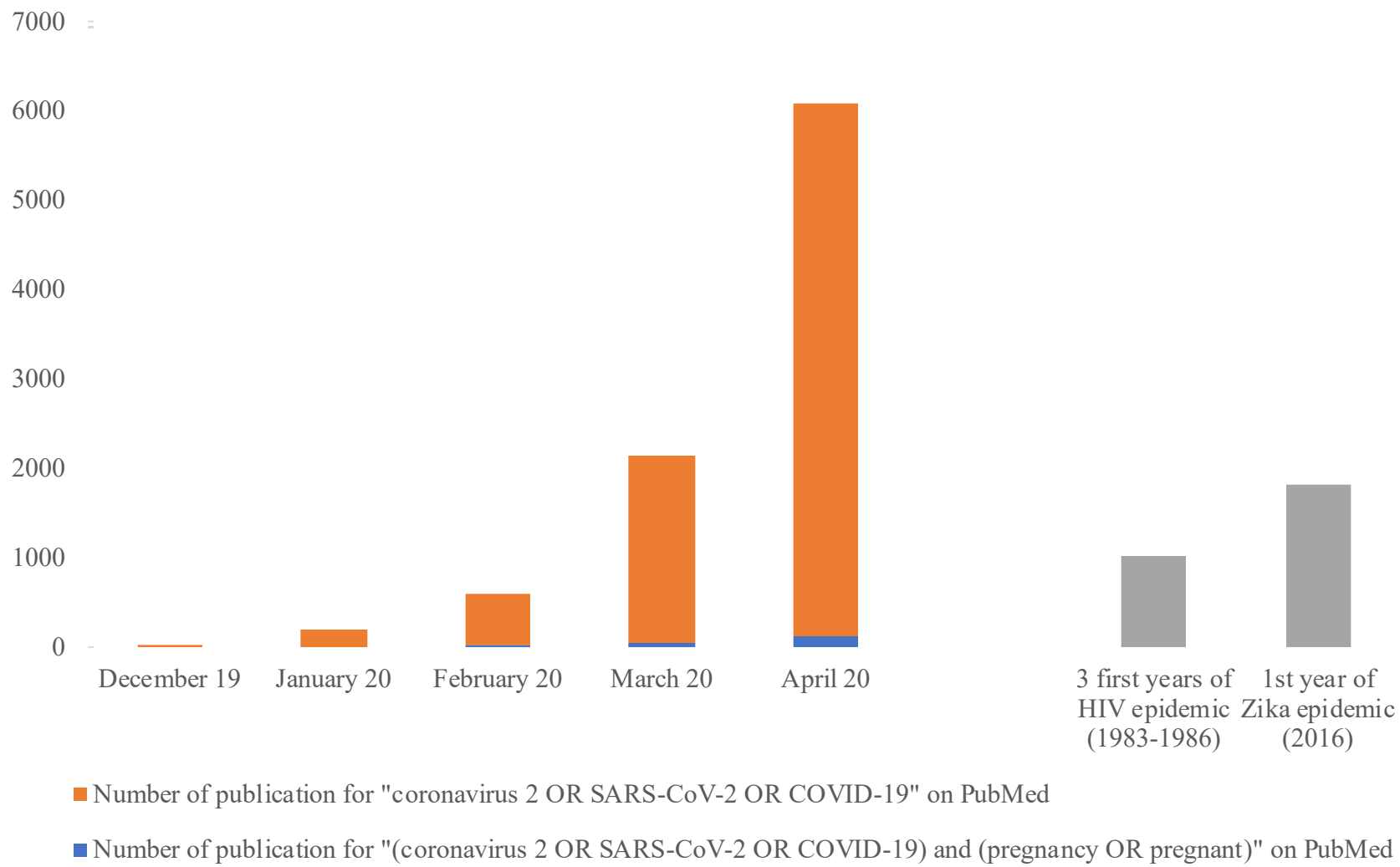
January 23th: 1st case confirmed in USA.

January 30th: WHO declared a Public Health Emergency of International Concern.

February 11th: WHO named the SARS-cov2 disease COVID-19.

March 11th: WHO declares the situation as a pandemic.

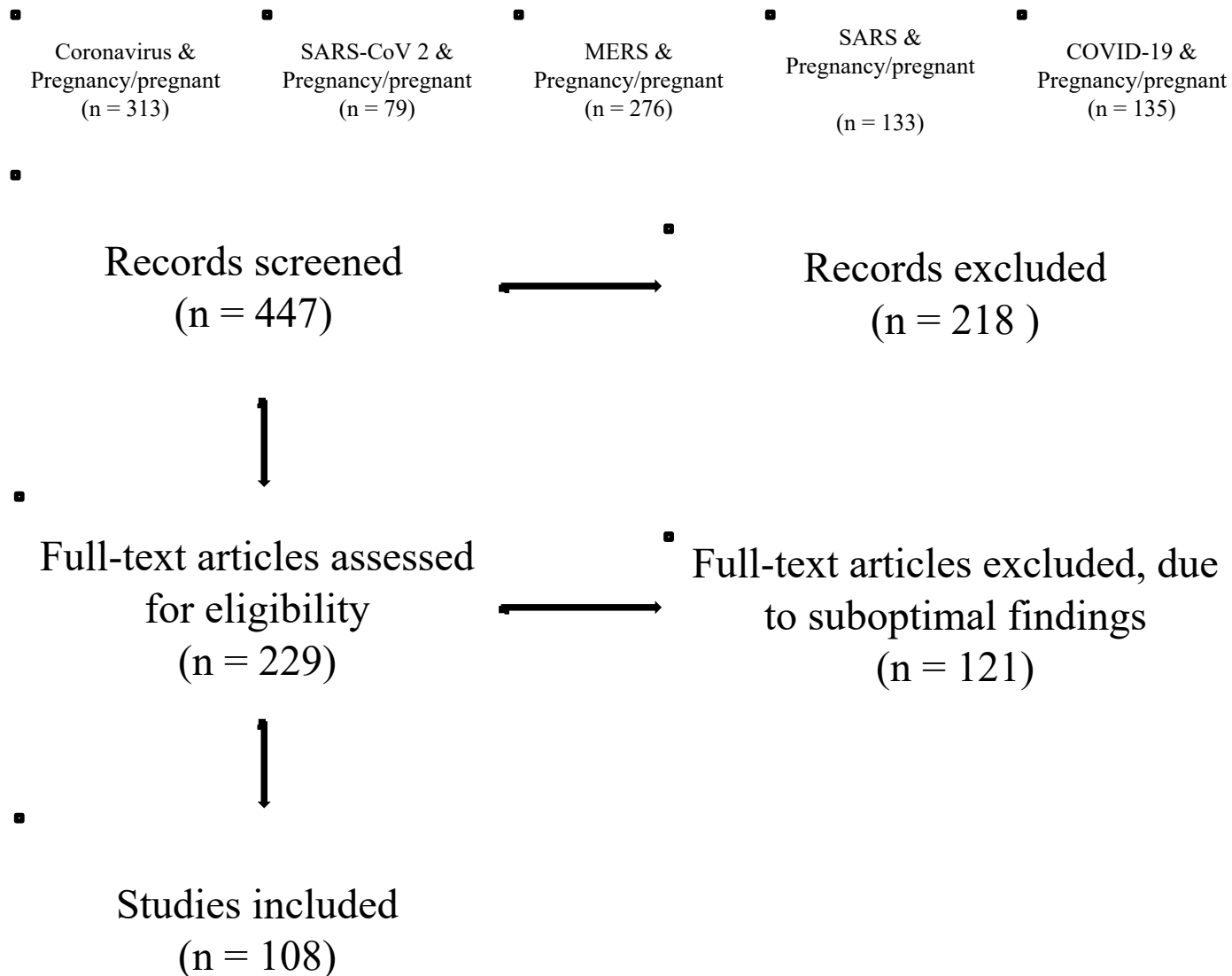
Number of publication for SARS-CoV-2, HIV and Zika virus





Prenatal Diagnosis

## PubMed search up to April 22, 2020



**Annexe 1. Publications for: “(COVID-19 OR SARS-Cov2 OR coronavirus) and (pregnancy OR pregnant)” research on PubMed on 22 April 2020.**

	<b>Author / Title</b>	<b>Type of research</b>	<b>Journal</b>	<b>Number of patients</b>	<b>Comments</b>
<b>1</b>	Peng Z, Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report	Case report	Journal of infection and Public Health	1	The nucleic acid test from the mother's amniotic fluid, vaginal secretions, cord blood, placenta, serum, anal swab, and breast milk were also negative. The most comprehensively tested case reported to date confirmed that the vertical transmission of COVID is unlikely.
<b>2</b>	Alzamora MC, Severe COVID-19 during Pregnancy and Possible Vertical Transmission.	Case report	American journal of perinatology	1	The patient developed respiratory failure requiring mechanical ventilation on day 5 of disease onset. The patient underwent a cesarean delivery, and neonatal isolation was implemented immediately after birth, without delayed cord clamping or skin-to-skin contact. The neonatal nasopharyngeal swab, 16 hours after delivery, was positive for severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2).
<b>3</b>	Tekbali A, Pregnant versus non-pregnant SARS-CoV-2 and COVID-19 Hospital Admissions: The first 4 weeks in New York.	Case series	American journal of obstetrics and gynecology	21'980	We used data that were concurrently collected at a large hospital 30 group in New York State between March 2 and March 29, 2020. Routine SARS31 CoV-2 testing was not performed. Data included the week of admission, the 32 pregnancy status of the patient, and the SARS-CoV-2 status (positive or negative).

4	Kwiatkowski S, Why we should not stop giving aspirin to pregnant women during the COVID-19 pandemic.	Review	Ultrasound in Obstetrics & Gynecology	none	To our knowledge, there is insufficient data to suggest an increased risk between prophylactic use of low-dose aspirin and progression of COVID-19 infection in pregnant women at risk of placental complications.
5	Jamieson DJ, Obstetricians on the Coronavirus Disease 2019 (COVID-19) Front Lines and the Confusing World of Personal Protective Equipment.	Review	Obstetrics & Gynecology	none	Therefore, strict adherence to hand hygiene and consistent use of recommended personal protective equipment are cornerstones for reducing transmission. In addition, it is critical that health care professionals receive training on and practice correct donning (putting on) and doffing (removing) of personal protective equipment
6	Zamaniyan M, Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission.	Case report	Prenatal Diagnosis	1	In this present study, we presented a pregnant woman with severe COVID-19 pneumonia who delivered a healthy preterm baby with no evidence of COVID-19 in her 32 weeks of gestation. Her RT-PCR test for COVID-19 was positive for amniotic fluid sample and second neonate nasal and throat test, but negative for vaginal secretion or umbilical cord blood or first neonate test.
7	Dotters-Katz SK, Considerations for Obstetric Care during the COVID-19 Pandemic.	Review	American journal of perinatology	none	This review will discuss what is known about the virus as it relates to pregnancy and then consider management considerations based on these data.

8	Yang P, Clinical characteristics and risk assessment of newborns born to mothers with COVID-19.	Case report	Journal of clinical virology	7 (newborns)	The current data show that the infection of SARS-CoV-2 in late pregnant women does not cause adverse outcomes in their newborns, however, it is necessary to separate newborns from mothers immediately to avoid the potential threats.
9	Vlachodimitropoulou Koumoutsea E, COVID19 and acute coagulopathy in pregnancy.	Review	Journal of thrombosis and haemostasis	none	The laboratory derangements may be reminiscent of HELLP syndrome, and thus knowledge of the COVID19 relationship is paramount for appropriate diagnosis and management. In addition to routine measurements of D-dimers, prothrombin time, and platelet count in all patients presenting with COVID19 as per ISTH guidance, monitoring of APTT and fibrinogen levels should be considered in pregnancy, as highlighted in this report.
10	Li L, Reply to "CT Findings of Pregnant Women With Coronavirus Disease (COVID-19) Pneumonia".	Reply	American journal of roentgenology	none	We thank Moradi et al. [1] for their interest in our article "Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis" [2] and their efforts to point out the error in Table 3. After consideration of the information presented by Moradi et al., we have corrected the contents of Table 3
11	Chen L, Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China.	Case report	The New England journal of medicine	118	We extracted information regarding epidemiologic, clinical, laboratory, and radiologic characteristics, treatment, and outcomes of pregnant women with Covid-19 through the epidemic reporting system of the National Health Commission of China, which stores the medical records of all 50 designated hospitals in Wuhan city.

12	Della Gatta AN, COVID19 during pregnancy: a systematic review of reported cases.	Systematic review	American Journal of Obstetrics and Gynecology	51	Although vertical transmission of SARS-Cov2 has been excluded thus far and the outcome for mothers and fetuses has been generally good, the high rate of preterm cesarean delivery is a reason for concern. These interventions were typically elective, and it is reasonable to question whether they were warranted or not.
13	Monteleone PA, A review of initial data on pregnancy during the COVID-19 outbreak: implications for assisted reproductive treatments.	Review	JBRA assisted reproduction	none	Reported data suggest that symptoms in pregnant women are similar to those in other people, and that there is no evidence for higher maternal or fetal risks
14	Li L, Follow-Up Information About the Four Pregnant Patients With Coronavirus Disease (COVID-19) Pneumonia Who Were Still in the Hospital at the End of Our Study.	Case report	American journal of roentgenology	4	Our observations in our article and this letter provide a basis for guidelines on monitoring and treatment of pregnant women with confirmed COVID-19 pneumonia. Our findings indicate that treatment of pregnant women with antiviral drugs, which are associated with potential risks to the fetus, may not be a prerequisite for recovery from COVID-19 pneumonia.

15	LaCourse SM, Importance of inclusion of pregnant and breastfeeding women in COVID-19 therapeutic trials.	Review	Clinical infectious diseases	none	In this Viewpoint, we call attention to the need and urgency to engage pregnant women in COVID-19 treatment trials now in order to develop data-driven recommendations regarding the risks and benefits of therapies in this unique but not uncommon population.
16	Yang H, Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019.	Case report	Journal of infection	55	The clinical symptoms and laboratory indicators are not obvious for asymptomatic and mild COVID-19 pregnant women. Pulmonary CT scan plus blood routine examination are more suitable for finding pregnancy women with asymptomatic or mild COVID-19 infection, and can be used screening COVID-19 pregnant women in the outbreak area of COVID-19 infection.
17	Breslin N, COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals.	Case report	American journal of obstetrics & gynecology MFM	43	We now describe a series of 43 test-confirmed cases of COVID-19 presenting to a pair of affiliated New York City hospitals over two weeks from March 13 to 27, 2020.

18	Di Mascio D, Outcome of Coronavirus spectrum infections (SARS, MERS, COVID 1 -19) during pregnancy: a systematic review and meta-analysis.	Systematic review and meta-analysis	American journal of obstetrics & gynecology MFM	79	In mothers infected with coronavirus infections, including COVID-19, >90% of whom also had pneumonia, PTB is the most common adverse pregnancy outcome. Miscarriage, preeclampsia, cesarean, and perinatal death (7- 11%) were also more common than in the general population. There have been no published cases of clinical evidence of vertical transmission
19	Omer S, Preventive measures and management of COVID-19 in pregnancy.	Review	Drugs & therapy perspectives	none	This commentary reviews the available information on managing COVID-19 during pregnancy to preserve the health of mothers and children in this critical situation.
20	Mayor S, Covid-19: Nine in 10 pregnant women with infection when admitted for delivery are asymptomatic, small study finds.	Comment	The BMJ	none	Nearly 90% of pregnant women admitted to hospital for delivery who test positive for SARS-CoV-2 have no symptoms of the infection, a small study has found
21	Moradi B, CT Findings of Pregnant Women With Coronavirus Disease (COVID- 19) Pneumonia.	Letter	American journal of roentgenology	none	It seems that the data in the second and third columns in Table 3 have been transposed, which needs correction.

22	Joseph Davey D, Contracting HIV or Contracting SARS-CoV-2 (COVID-19) in Pregnancy? Balancing the Risks and Benefits.	Notes	AIDS and behavior	none	Given the evidence and our experience, we argue that the benefits outweighs the risks in pregnant women and advocate for continued PrEP provision and HIV risk reduction counselling in HIV-uninfected pregnant and breastfeeding women at high-risk of HIV acquisition in South Africa.
23	Karami P, Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings.	Case report	Travel medicine and infectious disease	1	This report highlights details on a pregnant case of COVID-19 who unfortunately did not survive. This 27-year-old woman at her 30 and 3/7 weeks' gestation was referred to our center with fever, myalgia, and cough. The laboratory investigations showed leukopenia and lymphopenia as well as increased creatinine and CRP levels.
24	Ashokka B, Care of the Pregnant Woman with COVID-19 in Labor and Delivery: Anesthesia, Emergency cesarean delivery, Differential diagnosis in the acutely ill parturient, Care of the newborn, and Protection of the healthcare personnel.	Review	American journal of obstetrics & gynecology MFM	none	We present here the best evidence available to address many of these challenges, from making the diagnosis in symptomatic cases, to the debate between nucleic acid testing and chest imaging, to the management of the unwell patient in labor.



25	Khan S, Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth.	Case report	Infection control and hospital epidemiology	3	We report a case report study of 3 pregnant women with laboratory-confirmed COVID-19 pneumonia. All 3 pregnant women had vaginal deliveries. These patients presented with symptoms manifested by people with COVID-19.2 Of 3 patients, only 1 patient delivered a preterm baby.
26	Saccone G, The novel coronavirus (2019-nCoV) in pregnancy: What we need to know.	Review	European journal of obstetrics, gynecology, and reproductive biology	none	In conclusion, strict monitoring of women with suspected 2019-nCoV is firmly recommended. Obstetricians should promptly recognize the symptoms of 2019-nCoV, and adequately assess severity and fetal well-being.
27	Martinez-Portilla RJ, A Spanish-translated clinical algorithm for management of suspected SARS-CoV-2 infection in pregnant women.	Special article: algorithm translated	The Lancet. Infectious disease	none	With interest, we read the guidelines by Guillaume Favre and colleagues <sup>1</sup> on the management of pregnant women with suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Therefore, we propose a translated algorithm for Spanish-speaking countries (appendix). We also suggest that the new breastfeeding recommendations and the option to use dexamethasone as an alternative to betamethasone are adopted in Latin America.

28	Khan S, Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women.	Case series	Clinical microbiology and infection	17	In summary, we found two neonates suspected for COVID-19 infection and five neonates with neonatal pneumonia, suggesting the possibility that adverse pregnancy outcomes may be linked to COVID-19 infection.
29	Shah PS, Classification system and case definition for SARS-CoV-2 infection in pregnant women, fetuses, and neonates.	Review	Acta obstetrica et gynecologica Scandinavica	none	At present the evidence for intrauterine transmission from mother to fetus or intrapartum transmission from mother to the neonate is sparse. There are limitations associated with sensitivity and specificity of diagnostic tests used and classification of patients based on test results has also been questioned.
30	Deprest J, Feto-placental surgeries during the covid-19 pandemic: starting the discussion.	Review	Prenatal Diagnosis	none	Fetal diagnosis and pregnancy care need to be maintained, and we should strive to protect the vulnerable population of pregnant women as well as their fetus, as much as possible. This includes both SARS-CoV2-negative and positive patients with fetal anomalies that may benefit from prenatal intervention.
31	Mimouni F, Perinatal aspects on the covid-19 pandemic: a practical resource for perinatal- neonatal specialists.	Review	Journal of Perinatology	none	Vertical transmission from maternal infection during the third trimester probably does not occur or likely it occurs very rarely. Consequences of COVID-19 infection among women during early pregnancy remain unknown. We cannot conclude if pregnancy is a risk factor for more severe disease in women with COVID-19. Little is known about disease severity in neonates, and from very few samples, the presence of SARS-CoV-2 has not been documented in human milk.

32	Wilson AN, Caring for the carers: Ensuring the provision of quality maternity care during a global pandemic.	Review	Women and birth	none	This article provides an overview of important considerations for supporting the emotional, mental and physical health needs of maternity care providers in the context of the unprecedented crisis that COVID-19 presents. Cooperation, planning ahead and adequate availability of PPE is critical. Thinking about the needs of maternity providers to prevent stress and burnout is essential.
33	Palatnik A, Protecting Labor and Delivery Personnel from COVID-19 during the Second Stage of Labor.	Review	American journal of perinatology	none	We recommend that labor and delivery personnel have the utmost caution and be granted the protection they need to protect themselves and other patients. This includes providing labor and delivery personnel full PPE including N95 for the second stage of labor. This is critical to ensure the adequate protection for health care workers and to prevent spread to other health care workers and patients.
34	Xiong X, Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19.	Case report	Journal of medical virology	1	We report a case of a convalescing pregnant woman diagnosed as COVID-19 infection 37 days before delivery in the third trimester. A live birth without SARS-CoV-2 infection was delivered successfully via the vagina. Findings from our case indicate that there is no intrauterine transmission in this woman who develops COVID-19 pneumonia in late pregnancy.

35	Kranke P, [Obstetric Anesthesia During the SARS-CoV-2 Pandemic - a Brief Overview of Published Recommendations for Action by National and International Specialist Societies and Committees]. Article in German	Review	Anästhesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie : AINS	none	In summary, at present it must be stated that the general care recommendations that also apply to non-COVID-19 patients are initially valid with regard to obstetric anesthesia. Nevertheless, the special requirements on the part of hygiene and infection protection result in special circumstances that should be taken into account when caring for pregnant patients from an anesthetic point of view.
36	McIntosh JJ, Corticosteroid Guidance for Pregnancy during COVID-19 Pandemic.	Review	American journal of perinatology	none	It is necessary that obstetricians adjust practice to carefully weigh the fetal benefits with maternal risks. Therefore, our institution has examined the risks and benefits and altered our corticosteroid recommendations.
37	Gonzalez-Brown VM, Operating Room Guide for Confirmed or Suspected COVID-19 Pregnant Patients Requiring Cesarean Delivery.	Review	American journal of perinatology	none	This is a suggested protocol which may not be applicable to all health care settings but can be adapted to local resources and limitations of individual L&D units.

38	Parazzini F, Delivery in pregnant women infected with SARS-CoV-2: A fast review.	Review	International journal of gynaecology and obstetrics	64	The rate of vertical or peripartum transmission of SARS-CoV-2 is low, if any, for cesarean delivery; no data are available for vaginal delivery. Low frequency of spontaneous preterm birth and general favorable immediate neonatal outcome are reassuring.
39	Huang X, Epidemiology and Clinical Characteristics of COVID-19.	Review	Archives of Iranian medicine	none	The basic strategy for controlling the epidemic is early detection, early isolation, early diagnosis and early treatment. COVID-19 cases are insidious and transmissible in the incubation period, and multiple clusters have been reported in China. The causal role of COVID-19 in these cases is therefore uncertain and larger studies are needed in the future to describe the prevalence, clinical characteristics and course of the disease.
40	Pérez-López FR, Severe acute respiratory syndrome coronavirus 19 and human pregnancy.	Review	Gynecological endocrinology	none	Outcomes of pregnant women delivering in the upcoming months will provide more information on this particular new disease and its relation to pregnancy. In the meantime, it seems best that women should be encouraged to delay becoming pregnant until more evidence related to risks associated to COVID-19 infection during pregnancy is available. In addition, women susceptible to be submitted to assisted reproductive technology should take some additional precautions as recently recommended by La Marca et al.
41	Kowalski LP, COVID-19 pandemic: Effects and evidence-based recommendations for otolaryngology and head and neck surgery practice.	Review	Head & neck	none	This review summarizes some of the more readily available clinical protocols for head and neck specialists caring for patients in an environment of a SARS CoV-2 mediated COVID-19 pandemic. Recommendations are based largely on relatively small series, often from single centers, and national position statements. Some represent expert opinion and application from experiences with other diseases.

42	Wu X, Radiological findings and clinical characteristics of pregnant women with COVID-19 pneumonia.	Case report	International journal of gynaecology and obstetrics	23	Radiological findings and clinical characteristics in pregnant women with COVID-19 were similar to those of non-pregnant women with COVID-19. Median absorption time and length of hospitalization in asymptomatic patients were significantly shorter than in symptomatic patients. Lymphocyte percentage and neutrophil granulocyte rate may be used as laboratory indicators of CT absorption.
43	Du L, [Investigation on demands for antenatal care services among 2 002 pregnant women during the epidemic of COVID-19 in Shanghai]. Article in Chinese	Cross sectional study	Zhonghua fu chan ke za zhi	2002	Pregnant women in Shanghai critically concern about the risk of 2019-nCoV infections, and highly demand knowledge and measures on prevention and protection from COVID-19. They ask for having time-lapse appointments for ANC and online access to health information and services. Maternal and child care institutes should understand the demands of pregnant women, optimize the means of ANC service, and provide tailored and accessible health education and service for the safety of mother and child.
44	Sun LL, [Perioperative management of cesarean section for pregnant women with suspected or confirmed COVID-19]. Article in Chinese	Review	Zhonghua fu chan ke za zhi	none	It is recommended that the content involves preoperative preparation, surgery and anesthesia, postoperative management, and issues that need attention. It is for reference by fellow practitioners, and I hope it will be helpful.

45	Pu J, [Systematic perinatal management of the pregnant women and neonates during the epidemic of COVID-19]. Article in Chinese	Review	Zhonghua fu chan ke za zhi	none	This article puts forward targeted suggestions on the whole prevention and control of perinatal period for reference.
46	National Center for Health Care Quality Management in Obstetrics, [Suggestions on delivery management of pregnant women with COVID-19]. Article in Chinese	Review	Zhonghua fu chan ke za zhi	none	On the basis of more knowledge in this regard, combined with the experience from the front line of Wuhan, this article recommends the delivery management of pregnant women with suspected or confirmed COVID-19, hoping to play a greater role in promoting the current obstetric clinical work.
47	Chandrasekharan P, Neonatal Resuscitation and Postresuscitation Care of Infants Born to Mothers with Suspected or Confirmed SARS-CoV-2 Infection.	Special article: guidelines	American journal of perinatology	none	The manuscript outlines the precautions and steps to be taken before, during, and after resuscitation of a newborn born to a COVID-19 mother, including three optional variations of current standards involving shared-decision making with parents for perinatal management, resuscitation of the newborn, disposition, nutrition, and postdischarge care. The availability of resources may also drive the application of these guidelines.

48	Bourne T, ISUOG Consensus Statement on rationalization of gynecological ultrasound services in context of SARS-CoV-2.	Special article: guidelines	Ultrasound in obstetrics & gynecology	none	Given the challenges of the current coronavirus (SARS-CoV-2) pandemic and to protect both patients and ultrasound providers (physicians, sonographers, allied professionals), the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) has compiled the following expert-opinion-based guidance for the rationalization of ultrasound investigations for gynecological indications.
49	Bourne T, ISUOG Consensus Statement on rationalization of early-pregnancy care and provision of ultrasonography in context of SARS-CoV-2.	Special article: guidelines	Ultrasound in obstetrics & gynecology	none	This statement provides proposals and options for managing patients referred for assessment by early-pregnancy healthcare practitioners during the coronavirus disease 2019 (COVID-19) pandemic.
50	Mahony R, Pregnancy and Sars-Cov-2: A Novel Virus in a Unique Population	Comment	Irish medical journal	none	Comment about “Can SARS-CoV-2 Infection Be Acquired In Utero?: More Definitive Evidence Is Needed.”Kimberlin DW.
51	Ferrazzi EM, COVID-19 Obstetrics Task Force, Lombardy, Italy: executive management summary and short report of outcome.	Case report	International journal of gynaecology and obstetrics	42	An interim analysis of cases occurring in or transferred to these hubs was performed on March 20, 2020 and recommendations were released on March 24, 2020.



52	Chen Y, Infants Born to Mothers With a New Coronavirus (COVID-19).	Case report	Frontiers in pediatrics	4	Four full-term, singleton infants were born to pregnant women who tested positive for COVID-19 in the city of Wuhan, the capital of Hubei province, China, where the disease was first identified. Of the three infants, for who consent to be diagnostically tested was provided, none tested positive for the virus.
53	Wu C, Clinical Manifestation and Laboratory Characteristics of SARS-CoV-2 Infection in Pregnant Women.	Case report	Virologica Sinica	8	Here, we retrospectively analyzed the clinical features, laboratory characteristics, and imaging features of eight pregnant cases of SARS-CoV-2 infection during the pre-partum and post-partum periods. Our results showed that four of the eight pregnant women were asymptomatic before delivery but became symptomatic post-partum.
54	González Romero D, [Pregnancy and perinatal outcome of a woman with COVID-19 infection]. Article in Spanish	Case report	Revista clínica española	1	This article present a case of preganant woman infected by SARS-CoV 2. They propose some guidelines.
55	Bauer M, Obstetric Anesthesia During the COVID-19 Pandemic.	Review	Anesthesia and analgesia	none	The goal of this review is to provide evidence-based recommendations, or expert opinion when evidence is limited, for anesthesiologists caring for pregnant women during the COVID 19 pandemic, with a focus on preparedness and best clinical obstetric anesthesia practice.
56	Morand A, COVID-19 virus and children: What do we know?	Review	Archives of pediatrics	none	The COVID-19 virus seems to cause benign infections in children. The reasons for this tolerance are unknown. Currently, it is not clear whether specific pediatric populations (children with chronic disease or immunosuppressive treatment) will also have such a favorable outcome.

57	Gidlöf S, COVID-19 in pregnancy with comorbidities: More liberal testing strategy is needed	Letter to editor	Acta obstetrica et gynecologica Scandinavica	1	Potential difficulties in discriminating common complications encountered in high-risk pregnancies with comorbidities, such as pulmonary edema/embolism, from COVID-19.
58	Li N, Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study	Case control	Clinical infectious diseases	34	Severe maternal and neonatal complications were not observed in pregnant women with COVID-19 pneumonia who had vaginal delivery or caesarean section. Mild respiratory symptoms of pregnant women with COVID-19 pneumonia highlight the need of effective screening on admission.
59	Kalafat E, Lung ultrasound and computed tomographic findings in pregnant woman with COVID-19	Case report	Ultrasound in obstetrics & gynecology	1	Lung-ultrasound examination could play an important role in the triage of pregnant women with suspected COVID-19.
60	Sahu KK, A twin challenge to handle: COVID-19 with pregnancy	Letter to editor	Journal of medical virology	13	Pregnancy with COVID-19 disease is a special scenario that needs a good understanding of the pathophysiology of this disease.

<b>61</b>	Poon LC, Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals	Special article: guidelines	International journal of gynaecology and obstetrics	none	In response to the World Health Organization (WHO) statements and international concerns regarding the coronavirus disease 2019 (COVID-19) outbreak, FIGO has issued the following guidance for the management of pregnant women at the four main settings of pregnancy: (1) ambulatory antenatal care in the outpatient clinics; (2) management in the setting of the obstetrical triage; (3) intrapartum management; and (4) postpartum management and neonatal care. We also provide guidance on the medical treatment of pregnant women with COVID-19 infection.
<b>62</b>	Liu H, Why are pregnant women susceptible to COVID-19? An immunological viewpoint	Review article	Journal of Reproductive Immunology	18	Pregnant women are more susceptible to respiratory pathogens; hence, they may be more susceptible to COVID-19 infection than the general population.
<b>63</b>	Al-Tawfiq JA, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and COVID-19 infection during pregnancy.	Review article	Travel Medicine and Infectious Disease	none	Thus, similar to the difference in the clinical presentation and course among SARS, MERS-CoV and COVID-19, there is also differences in the outcome and course of pregnant women with these coronaviruses' infection.

64	Zhang B, Treatment with convalescent plasma for critically ill patients with SARS-CoV-2 infection	Case reports	CHEST	4 (including 1 pregnant woman)	Herein, we presented four critically ill patients with SARS-CoV-2 infection who received supportive care and convalescent plasma. Although all the four patients (including a pregnant woman) recovered from SARS-CoV-2 infection eventually, randomized trials are needed to eliminate the effect of other treatments and investigate the safety and efficacy of convalescent plasma therapy.
65	Davanzo R, Breastfeeding and Coronavirus Disease-2019. Ad interim indications of the Italian Society of Neonatology endorsed by the Union of European Neonatal & Perinatal Societies.	Review article	Maternal & child nutrition	none	If a mother previously identified as COVID-19 positive or under investigation for COVID-19 is asymptomatic or paucisymptomatic at delivery, rooming-in is feasible and direct breastfeeding is advisable, under strict measures of infection control. On the contrary, when a mother with COVID-19 is too sick to care for the newborn, the neonate will be managed separately and fed fresh expressed breast milk, with no need to pasteurize it, as human milk is not believed to be a vehicle of COVID-19.

<b>66</b>	Chawla D, Perinatal-Neonatal Management of COVID-19 Infection - Guidelines of the Federation of Obstetric and Gynecological Societies of India (FOGSI), National Neonatology Forum of India (NNF), and Indian Academy of Pediatrics (IAP)	Special article: Guidelines	Indian pediatrics	none	A set of twenty recommendations are provided under the following broad headings: 1) pregnant women with travel history, clinical suspicion or confirmed COVID-19 infection; 2) neonatal care; 3) prevention and infection control; 4) diagnosis; 5) general questions.
<b>67</b>	Karimi-Zarchi M, Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review.	Review article	Fetal and pediatric pathology	none	Currently, based on limited data, there is no evidence for intrauterine transmission of COVID-19 from infected pregnant women to their fetuses. Mothers may be at increased risk for more severe respiratory complications.
<b>68</b>	Panahi L, Risks of Novel Coronavirus Disease (COVID-19) in Pregnancy; a Narrative Review.	Narrative review	Archives of academic emergency medicine	none	A review of 13 final articles published in this area revealed that COVID-19 can cause fetal distress, miscarriage, respiratory distress and preterm delivery in pregnant women but does not infect newborns. It is necessary to monitor suspected pregnant women before and after delivery. For confirmed cases both the mother and the newborn child should be followed up comprehensively.

69	Lee DH, Emergency cesarean section on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) confirmed patient.	Case reports	Korean journal of anesthesiology	1	We report the first case of a SARS-CoV-2 positive woman delivering a baby through cesarean section at 37+6 weeks of pregnancy in the Republic of Korea. This case suggested that negative pressure operating room, skillful medical team, and enhanced personal protective equipment including N95 masks, surgical cap, double gown, double gloves, shoe covers, and powered air-purifying respirator are required at the hospital for safe delivery in such a case.
70	Mirzadeh M, Pregnant Women in the Exposure to COVID-19 Infection Outbreak: The Unseen Risk Factors and Preventive Healthcare Patterns.	Letter to Editor	The journal of maternal-fetal & neonatal medicine	none	A standard balance in self-care strategies and the adherence to diverse training guidelines mentioned in Internet-based guided self-help therapy (INSHT) not only can reduce/prevent the viral infection in pregnant women, but also can change the childbirth mode from cesarean to vaginal.
71	Zambrano LI, A pregnant woman with COVID-19 in Central America.	Case reports	Travel Medicine and Infectious Disease	1	On March 9, 2020, a 41-year-old female, who was 31 weeks pregnant, were diagnosed with COVID-19. In this case, her clinical presentation showed no significant alterations related to COVID-19. On March 19, occurred a preterm delivery, obtained by spontaneous vaginal delivery.
72	Chen S, Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia.	Case reports	Journal of medical virology	5	It is probable that pregnant women diagnosed with COVID-19 have no fever before delivery. Their primary initial manifestations were merely low-grade postpartum fever or mild respiratory symptoms. Therefore, the protective measures are necessary on admission; the instant CT scan and real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay should be helpful in early diagnosis and avoid cross-infection on the occasion that patients have fever and other respiratory signs.

73	Luo Y, Management of pregnant women infected with COVID-19.	Review article	The Lancet. Infectious diseases	none	As discussed in the study, although all mothers and infants showed good outcomes, all enrolled pregnant women were in the third trimester, and all had only mild symptoms. Hence, the effect of SARS-CoV-2 infection on the fetus in the first or second trimester or in patients with moderate to severe infection is unknown. We need to further strengthen research to provide an evidence-based foundation for the medical management of pregnant patients with COVID-19.
74	Yu N, Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study.	Retrospective study	The Lancet. Infectious diseases	7	The maternal, fetal, and neonatal outcomes of patients who were infected in late pregnancy appeared very good, and these outcomes were achieved with intensive, active management that might be the best practice in the absence of more robust data. The clinical characteristics of these patients with COVID-19 during pregnancy were similar to those of non-pregnant adults with COVID-19 that have been reported in the literature.
75	Qi H, Safe Delivery for COVID-19 Infected Pregnancies.	Commentary article	BJOG : an international journal of obstetrics and gynaecology	none	Care should be taken in determination of the timing of delivery, assessment of the indications for caesarean section, preparation of the delivery room to prevent infection, choice of the type of anesthesia, and newborn management.
76	Chen Y, Maternal health care management during the outbreak of coronavirus disease 2019 (COVID-19).	Case reports	Journal of medical virology	3	Given that 420 patients were diagnosed by Mar. 11th in Shenzhen and tens of cases was diagnosed in our hospital, yet no nosocomial infection has occurred and none of the pregnant woman registered in our hospital was reported to be infected, this management should be effective to an extent, however mathematical model may be needed to quantify the effectiveness of these methods.

77	Wang SS, Experience of Clinical Management for Pregnant Women and Newborns with Novel Coronavirus Pneumonia in Tongji Hospital, China.	Special article: Guidelines	Current medical science	none	On January 28, we published “Guidance for maternal and fetal management during pneumonia epidemics of novel coronavirus infection in the Wuhan Tongji Hospital (First edition)”[4]. Based on the clinical characteristics, diagnosis and treatment progress of the recently discovered diseases, we offered an updated clinical management for pregnant women and newborns with NCP.
78	Dashraath P, Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy.	Review article	American Journal of Obstetrics and Gynecology	none	Special precautions are required to minimize cross-infection of healthcare providers while performing procedures that require close physical contact and promote droplet exposure such as vaginal delivery. Much of the obstetric management is based on consensus and best practice recommendations as clinical efficacy data regarding anti-viral therapy and corticosteroid use is evolving.
79	Rasmussen SA, Coronavirus Disease 2019 (COVID-19) and Pregnancy: Responding to a Rapidly Evolving Situation.	Review article	Obstetrics and gynecology	none	Some current recommendations are well supported, based largely on what we know from seasonal influenza: patients should avoid contact with ill persons, avoid touching their face, cover coughs and sneezes, wash hands frequently, disinfect contaminated surfaces, and stay home when sick. Prenatal clinics should ensure all pregnant women and their visitors are screened for fever and respiratory symptoms, and symptomatic women should be isolated from well women and required to wear a mask.



<b>80</b>	Liao X, Chest CT Findings in a Pregnant Patient with 2019 Novel Coronavirus Disease.	Case report	Balkan medical journal	1	In this report, the chest CT characteristics of a pregnant woman with COVID-19 are presented from admission to recovery. The patient showed mild clinical symptoms. She was confirmed to have COVID-19 based on a positive nucleic acid test and typical viral infection signs in the lungs observed by CT. The observations in this case suggested that the clinical symptoms of COVID-19 can be inconsistent with the CT examination results.
<b>81</b>	Giwa AL, Novel 2019 coronavirus SARS- CoV-2 (COVID- 19): An updated overview for emergency clinicians	Review article	Emergency medicine practice	none	Clearly, larger studies will need to be conducted to better evaluate the risk of vertical transmission between mother and fetus with SARS-CoV-2 infection.
<b>82</b>	Kang X, Anesthesia management in cesarean section for a patient with coronavirus disease 2019	Case report	Journal of Zhejiang University. Medical sciences	1	For ordinary COVID-19 patients intraspinal anesthesia is preferred in cesarean section, and the influence on respiration and circulation in both maternal and infant should be reduced; while for severe or critically ill patients general anesthesia with endotracheal intubation should be adopted. The safety of medical environment should be ensured, and level-III standard protection should be taken for anesthetists. Special attention and support should be given to maternal psychology.
<b>83</b>	Moro F, How to perform lung ultrasound in pregnant women with suspected COVID-19 infection.	Review article	Ultrasound in obstetrics & gynecology	none	We propose a practical approach for obstetricians/gynecologists to perform lung ultrasound, showing potential applications, semiology and practical aspects, which should be of particular importance in emergency situations, such as the current pandemic infection of COVID-19.

<b>84</b>	Rimmer A, Covid-19: doctors in final trimester of pregnancy should avoid direct patient contact.	Special article: News	British medical journal	none	Women who are more than 28 weeks pregnant should avoid direct contact with patients—whether or not they could be infected with covid-19, says updated guidance. The advice comes from updated guidance from the Royal College of Obstetricians and Gynaecologists (RCOG), the Royal College of Midwives, and the Royal College of Paediatrics and Child Health.
<b>85</b>	Peyronnet V, SARS-CoV-2 infection during pregnancy. Information and proposal of management care. CNGOF	Special article: Guidelines	Gynécologie, obstétrique, fertilité & sénologie	none	Pregnancy is known as a period at higher risk for the consequences of respiratory infections, as for influenza, so it seems important to screen for Covid-19 in the presence of symptoms and to monitor closely pregnant women. In this context of the SARS-Covid-2 epidemic, the societies of gynecology-obstetrics, infectious diseases and neonatology have proposed a French protocol for the management of possible and proven cases of SARS-Covid-2 in pregnant women.
<b>86</b>	Wen R, A patient with SARS-CoV-2 infection during pregnancy in Qingdao, China.	Case reports	Journal of microbiology, immunology, and infection	1	A 31-year-old female at 30 weeks gestation presented with mild diarrhea (2-3 times a day) for one day. Combined PCR and CT, she was diagnosed as pregnancy with COVID-19. She made a recovery and discharged on Feb 20. The fetus developed normally and wasn't birth during hospitalization.
<b>87</b>	Schmid MB, COVID-19 in pregnant women.	Review article	The Lancet. Infectious disease	none	Therefore, as long as national authority guidelines or evidence-based recommendations do not yet exist, clinical practitioners need to screen the literature and review their actions on a daily basis.
<b>88</b>	Baud D, COVID-19 in pregnant women - Authors' reply.	Review article: Guidelines	The Lancet. Infectious disease	none	We therefore updated the guidelines according to the data available at the beginning of March, 2020 (appendix). It is our responsibility, as specialists working in different fields of perinatology, to improve our own recommendations and that of others for the benefit of our patients.

<b>89</b>	[Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition)] Article in Chinese	Special article: Guidelines	Chinese journal of contemporary pediatrics	none	The Working Group for the Prevention and Control of Neonatal SARS-CoV-2 Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics worked out the perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (1st Edition).
<b>90</b>	Wang LS, An interpretation on perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition) Article in Chinese	Special article: Guidelines	Chinese journal of contemporary pediatrics	none	Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition) has been worked out by the Editorial Committee of Chinese Journal of Contemporary Pediatrics.
<b>91</b>	Chen D, Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection.	Special article: Guidelines	International journal of gynaecology and obstetrics	none	Ten key recommendations were provided for the management of COVID-19 infections in pregnancy.

92	Zhou D, COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression.	Review article	The Journal of antimicrobial chemotherapy	none	In summary, we propose that hydroxychloroquine (HCQ) could serve as a better therapeutic approach than chloroquine (CQ) for the treatment of SARS-CoV-2 infection. There are three major reasons for this: (i) HCQ is likely to attenuate the severe progression of COVID-19 through inhibiting the cytokine storm by reducing CD154 expression in T cells; (ii) HCQ may confer a similar antiviral effect at both pre- and post- infection stages, as found with CQ; (iii) HCQ has fewer side effects, is safe in pregnancy and is cheaper and more highly available in China.
93	Sahu KK, COVID-2019 and Pregnancy: A plea for transparent reporting of all cases.	Letter to Editor	Acta obstetricia et gynecologica Scandinavica	none	Transparent and comprehensive reporting of all cases of COVID-19 pregnancies is very important. We believe that building a common portal where details of all such cases could be entered continuously so that data analysis could be performed in real-time to get some concrete results helping to generate evidence and guide clinical management.
94	Rimmer A, Covid-19: pregnant doctors should speak to occupational health, say experts.	Special article: News	British medical journal	none	Government guidance advises people with an increased risk of severe illness from covid-19, including pregnant women, to be particularly stringent in following social distancing measures. No data currently suggest an increased risk of miscarriage or early pregnancy loss in relation to covid-19.
95	Liu D, Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis.	Review article	American journal of roentgenology	15	Pregnancy and childbirth did not aggravate the course of symptoms or CT features of COVID-19 pneumonia. All the cases of COVID-19 pneumonia in the pregnant women in our study were the mild type. All the women in this study—some of whom did not receive antiviral drugs—achieved good recovery from COVID-19 pneumonia.

<b>96</b>	Rashidi Fakari F, Coronavirus Pandemic and Worries during Pregnancy; a Letter to Editor.	Letter to Editor	Archives of academic emergency medicine	none	Increasing mothers' awareness about the transmission of Coronavirus, risk factors, and red flags, as well as providing tele-counseling for pregnancy care and tele-triage could help reduce their anxiety and worry. It is also recommended that in cities where home birth and home services after birth are available, the medical team provide these services at home while maintaining safety.
<b>97</b>	Fan C, Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry?	Case reports	Clinical infectious diseases	2	We presented two cases of COVID-19 associated SARS-CoV-2 infection during third trimester of pregnancy. Both mothers and newborns had excellent outcomes. We failed to identify SARS-CoV-2 in all the products of conception and the newborns. This report provided evidence of low risk of intrauterine infection by vertical transmission of SARS-CoV-2.
<b>98</b>	Jiao J, Under the epidemic situation of COVID-19, should special attention to pregnant women be given?	Review article	Journal of medical virology	none	More data and experience is still needed to be collected for confirming the transmission and clinical characteristics of pregnancy. There is no recommendation for routine detection and monitoring of early and midterm pregnancy, but such follow ups may need to be further strengthened. Pregnant medical staff should be supported by policy.

99	Schwartz DA, An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes.	Case reports	Archives of pathology & laboratory medicine	38	This analysis reveals that unlike coronavirus infections of pregnant women caused by SARS and MERS, in these 38 pregnant women COVID-19 did not lead to maternal deaths. Importantly, and similar to pregnancies with SARS and MERS, there were no confirmed cases of intrauterine transmission of SARS-CoV-2 from mothers with COVID-19 to their fetuses. All neonatal specimens tested, including in some cases placentas, were negative by rt-PCR for SARS-CoV-2. At this point in the global pandemic of COVID-19 infection there is no evidence that SARSCoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses.
100	Mullins E, Coronavirus in pregnancy and delivery: rapid review.	Review article	Ultrasound in obstetrics & gynecology	32	Serious morbidity occurred in 2/32 women with COVID-19, both of whom required ICU care. Compared with SARS and MERS, COVID-19 appears less lethal, acknowledging the limited number of cases reported to date and that one woman remains in a critical condition. Preterm delivery affected 47% of women hospitalized with COVID-19. Based on this review, RCOG, in consultation with RCPCH, developed guidance for delivery and neonatal care in pregnancies affected by COVID-19, which recommends that delivery mode be determined primarily by obstetric indication and recommends against routine separation of affected mothers and their babies.

<b>101</b>	Chen R, Safety and efficacy of different anesthetic regimens for parturients with COVID-19 undergoing Cesarean delivery: a case series of 17 patients.	Case reports	Canadian journal of anaesthesia	17	Both epidural and general anesthesia were safely used for Cesarean delivery in the parturients with COVID-19. Nevertheless, the incidence of hypotension during epidural anesthesia appeared excessive. Proper patient transfer, medical staff access procedures, and effective biosafety precautions are important to protect medical staff from COVID-19.
<b>102</b>	Liu H, Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children.	Case reports	Journal of Infection	59 (including 16 laboratory-confirmed and 25 clinically-diagnosed pregnant women)	Atypical clinical findings of pregnant women with COVID-19 could increase the difficulty in initial identification. Consolidation on CT was more common in the pregnant groups. The clinically-diagnosed cases were vulnerable to more pulmonary involvement. CT was the modality of choice for early detection, severity assessment, and timely therapeutic effects evaluation for the cases with epidemic and clinical features of COVID-19 with or without laboratory confirmation.
<b>103</b>	Wang S, A case report of neonatal COVID-19 infection in China.	Case reports	Clinical Infectious Disease	1	We report the first case of neonatal SARS-CoV-2 infection in China where the mother was confirmed with COVID-19. The clinical manifestations of the mother and the baby were both mild and the baby's prognosis was good. Whether the case is intrauterine vertical transmission or not remains controversial.
<b>104</b>	Stower H, Lack of maternal-fetal SARS-CoV-2 transmission.	Review article	Nature medicine	none	Chen et al. studied nine pregnant women with lab-confirmed COVI-19 who were admitted to the Zhongnan Hospital of Wuhan University. They found that their clinical symptoms were similar to those of non-pregnant adults and that there was no indication of vertical transmission to children, although the findings need to be confirmed in a larger study.

<b>105</b>	Poon LC, ISUOG Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals.	Special article: Guidelines	Ultrasound in obstetrics & gynecology	none	In response to the World Health Organization (WHO) statements and international concerns regarding the novel coronavirus infection (COVID-19) outbreak, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) is issuing the following guidance for management during pregnancy and puerperium.
<b>106</b>	Zhu H, Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia.	Case reports	Translational pediatrics	10 (neonates)	Perinatal 2019-nCoV infection may have adverse effects on newborns, causing problems such as fetal distress, premature labor, respiratory distress, thrombocytopenia accompanied by abnormal liver function, and even death. However, vertical transmission of 2019-nCoV is yet to be confirmed.
<b>107</b>	Chen H, Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records.	Case reports	The Lancet	9	The clinical characteristics of COVID-19 pneumonia in pregnant women were similar to those reported for non-pregnant adult patients who developed COVID-19 pneumonia. Findings from this small group of cases suggest that there is currently no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy.
<b>108</b>	Qiao J, What are the risks of COVID-19 infection in pregnant women?	Comment	The Lancet	none	Pregnant women and newborn babies should be considered key at-risk populations in strategies focusing on prevention and management of COVID-19 infection.



<b>109</b>	Zhang L, [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Article in Chinese.	Case reports	Zhonghua fu chan ke za zhi	10 (neonates)	If there is an indication for obstetric surgery or critical illness of COVID-19 in pregnant women, timely termination of pregnancy will not increase the risk of premature birth and asphyxia of the newborn, but it is beneficial to the treatment and rehabilitation of maternal pneumonia. Preventive use of long-acting uterotonic agents could reduce the incidence of postpartum hemorrhage during surgery. 2019-nCoV infection has not been found in neonates delivered from pregnant women with COVID-19.
<b>110</b>	Liu Y, Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy.	Case reports	Journal of infection	13	The report showed pregnant women are also susceptible to SARS-CoV-2 infection. SARS-CoV-2 may increase health risks to both mothers and infants during pregnancy. Efforts should be taken to reduce the infection rate of SARS-CoV-2 both in pregnant and perinatal period, and more intensive attention should be paid to pregnant patients.
<b>111</b>	Favre G, Guidelines for pregnant women with suspected SARS-CoV-2 infection.	Special article: Guidelines	The Lancet. Infectious disease	none	Pregnant women with laboratory-confirmed SARS-CoV-2 infection who are asymptomatic should be self-monitored at home for clinical features of COVID-19 for at least 14 days. Newborns of mothers positive for SARS-CoV-2 should be isolated for at least 14 days or until viral shedding clears, during which time direct breastfeeding is not recommended.
<b>112</b>	Liang H, Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow?	Special article: Guidelines	Acta obstetricia et gynecologica Scandinavica	none	A multi-disciplinary team approach should be adopted in managing these patients as it allows to effectively share the expertise as well as responsibility, and treat our patients with dignity and compassion. In hospitals, the transmission of the virus and deaths among healthcare professionals are serious concerns. Improving healthcare governance, as well as supporting, educating and training healthcare personnel in infection control and self-protection need to be prioritized.

113	Cao Q, SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics.	Review article	Journal of the Formosan Medical Association	none	Perinatal infection can occur if the baby is born to a pregnant woman with confirmed infection via vaginal delivery.
114	Li Y, Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China.	Case report	Emerging infectious diseases	1	A woman with 2019 novel coronavirus disease in her 35th week of pregnancy delivered an infant by cesarean section in a negative-pressure operating room. The infant was negative for severe acute respiratory coronavirus 2. This case suggests that mother-to-child transmission is unlikely for this virus.
115	Yang H, Novel coronavirus infection and pregnancy.	Review article	Ultrasound in obstetrics & gynecology	none	Currently, there is no evidence that pregnant women are more susceptible to COVID-19 infection and that those with COVID-19 infection are more prone to developing severe pneumonia. There is also no evidence of vertical mother-to-baby transmission of COVID-19 infection when the maternal infection manifests in the third trimester.
116	Zaigham M, Maternal and Perinatal Outcomes with COVID-19: a systematic review of 108 pregnancies.	Review article	Acta obstetricia et gynecologica Scandinavica	108	Although the majority of mothers were discharged without any major complications, severe maternal morbidity as a result of COVID-19 and perinatal deaths were reported. Vertical transmission of the COVID-19 could not be ruled out. Careful monitoring of pregnancies with COVID-19 and measures to prevent neonatal infection are warranted.

117	Wang X, A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery.	Case report	Clinical infectious diseases	1	In this case, we reported that a mother with COVID-19 gave birth to a healthy baby with no evidence of COVID-19 during her 30 weeks pregnancy. Our case ended up with an uneventful postpartum and neonatal course. The RT-PCR tests were all negative, suggesting the infant was unaffected by COVID-19, and all healthcare workers taking care of him had remained asymptomatic.
118	Chen S, [Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases]. Article in Chinese.	Case reports	Chinese journal of pathology	3	The clinical characteristics of pregnant women with 2019-nCoV infection in late pregnancy are similar to those of non-pregnant patients, and no severe adverse pregnancy outcome is found in the 3 cases of our observation. Pathological study suggests that there are no morphological changes related to infection in the three placentas. Currently no evidence for intrauterine vertical transmission of 2019-nCoV is found in the three women infected by 2019-nCoV in their late pregnancy.
119	Rasmussen SA, Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know.	Review article	American journal of obstetrics and gynecology	none	Principles of management of coronavirus disease 2019 in pregnancy include early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, consideration of empiric antibiotics (secondary to bacterial infection risk), laboratory testing for the virus and coinfection, fetal and uterine contraction monitoring, early mechanical ventilation for progressive respiratory failure, individualized delivery planning, and a team-based approach with multispecialty consultations.

120	Catton H, Global challenges in health and health care for nurses and midwives everywhere.	Review article	International nursing review	none	The next decade is likely to produce any number of global challenges that will affect health and health care, including pan-national infections such as the new coronavirus COVID-19 and others that will be related to global warming. Nurses will be required to react to these events, even though they will also be affected as ordinary citizens. The future resilience of healthcare services will depend on having sufficient numbers of nurses who are adequately resourced to face the coming challenges.
121	Working Group for the Prevention and Control of Neonatal 2019-nCoV Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics. [Perinatal and neonatal management plan for prevention and control of 2019 novel coronavirus infection (1st Edition)]. Article in Chinese	Special article: Guidelines	Chinese journal of contemporary pediatrics	none	According to the latest 2019-nCoV national management plan and the actual situation, the Working Group for the Prevention and Control of Neonatal 2019-nCoV Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics puts forward recommendations for the prevention and control of 2019-nCoV infection in neonates.

122	Schwartz DA, Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections.	Review article	Viruses	none	In order to assess the potential of the Wuhan 2019-nCoV to cause maternal, fetal and neonatal morbidity and other poor obstetrical outcomes, this communication reviews the published data addressing the epidemiological and clinical effects of SARS, MERS, and other coronavirus infections on pregnant women and their infants.
123	Favre G, 2019-nCoV epidemic: what about pregnancies?	Review article	The Lancet	none	Considering that the 2019-nCoV seems to have a similar pathogenic potential as SARS-CoV and MERS-CoV, pregnant women are at increased risk of severe infections, there are no specific clinical signs of coronavirus infections preceding severe complications, coronaviruses have the potential to cause severe maternal or perinatal adverse outcomes, or both, and the current lack of data on the consequences of a 2019-nCoV infection during pregnancy, we recommend systematic screening of any suspected 2019-nCoV infection during pregnancy.

124	Langel SN, Host Factors Affecting Generation of Immunity Against Porcine Epidemic Diarrhea Virus in Pregnant and Lactating Swine and Passive Protection of Neonates.	Review article	Pathogens	none	NOT ABOUT CORONAVIRUS – 2 Porcine epidemic diarrhea virus (PEDV) is a highly virulent re-emerging enteric coronavirus that causes acute diarrhea, dehydration, and up to 100% mortality in neonatal suckling piglets. Because pregnancy-associated immune alterations influence viral pathogenesis and adaptive immune responses in many different species, a better understanding of host immune responses to PEDV in pregnant swine may translate into improved maternal immunization strategies against enteric pathogens for multiple species.
125	Hou Y, Emerging Highly Virulent Porcine Epidemic Diarrhea Virus: Molecular Mechanisms of Attenuation and Rational Design of Live Attenuated Vaccines.	Review article	International journal of molecular sciences	none	NOT ABOUT CORONAVIRUS – 2 PEDV belongs to the genus Alphacoronavirus within the family Coronaviridae. In the future, rationally designed PEDV LAV candidates bearing different genetic modifications should be evaluated in pregnant sows that are the major targets of PEDV vaccination, and can passively protect suckling piglets from PEDV disease via the PEDV-specific neutralizing antibodies in colostrum and milk.
126	De Castro A, Haemophilus parainfluenzae endocarditis with multiple cerebral emboli in a pregnant woman with coronavirus.	Case report	IDCases	1	The patient's presentation reinforces that neurological symptoms may be the presenting complaint in patients with endocarditis. Clinicians should maintain a high index of suspicion for IE when encountering patients presenting with neurological complaints in the setting of fever, given the potential for cerebrovascular complications, and the improved outcomes with timely initiation of appropriate antimicrobial therapy.

127	Won H, Generation and protective efficacy of a cold-adapted attenuated genotype 2b porcine epidemic diarrhea virus.	Review article	Journal of veterinary science	none	NOT ABOUT CORONAVIRUS – 2 Porcine epidemic diarrhea virus (PEDV) is a member of the genus Alphacoronavirus, belonging to in the family Coronaviridae of the order Nidovirales. This is the first report describing the development of a cold-adapted MLV vaccine based on a virulent G2b PEDV strain.
128	Wen Z, A heterologous 'prime-boost' anti-PEDV immunization for pregnant sows protects neonatal piglets through lactogenic immunity against PEDV.	Review article	Letters in applied microbiology	none	NOT ABOUT CORONAVIRUS – 2 Porcine epidemic diarrhoea virus (PEDV) causes severe diarrhoea in neonatal suckling piglets with a high mortality. Our data show that pregnant sows were immunized with 'coated PEDV-loaded microspheres + killed PEDV vaccines' (heterologous prime-boost immunization) could protect more than 90% suckling piglets delivered by the sows against the virus. These findings provide a new model of developing safe and effective immunizations for newborn animals against established and emerging enteric infections.
129	Tu CF, Lessening of porcine epidemic diarrhoea virus susceptibility in piglets after editing of the CMP-N-glycolylneuraminic acid hydroxylase gene with CRISPR/Cas9 to nullify N-glycolylneuraminic acid expression.	Review article	PloS one	none	NOT ABOUT CORONAVIRUS – 2 The porcine epidemic diarrhoea virus (PEDV) devastates the health of piglets but may not infect piglets whose CMP-N-glycolylneuraminic acid hydroxylase (CMAH) gene is mutated (knockouts, KO) by using CRISPR/Cas9 gene editing techniques. These results suggest that porcine CMAH KO with nullified NGNA expression are not immune to PEDV but that this KO may lessen the severity of the infection and delay its occurrence.

<b>130</b>	Huang X, Novel Gold Nanorod-Based HR1 Peptide Inhibitor for Middle East Respiratory Syndrome Coronavirus.	Review article	ACS applied materials & interfaces	none	NOT ABOUT CORONAVIRUS – 2 Middle East respiratory syndrome coronavirus (MERS-CoV) causes a severe acute respiratory syndrome-like illness with high pathogenicity and mortality due to the lack of effective therapeutics. In summary, PIH-AuNRs represent a novel class of antiviral agents and have a great potential in treating MERS in the clinic.
<b>131</b>	Jang G, Assessment of the safety and efficacy of an attenuated live vaccine based on highly virulent genotype 2b porcine epidemic diarrhea virus in nursing piglets.	Review article	Veterinary microbiology	none	NOT ABOUT CORONAVIRUS – 2 We have previously reported the generation of the attenuated KNU-141112-S DEL5/ORF3 virus by continuous propagation of highly virulent G2b porcine epidemic diarrhea virus (PEDV) in Vero cells. The data demonstrated that the attenuated S DEL5/ORF3 strain guarantees the safety to host animals with no reversion to virulence and is suitable as an effective primary live vaccine providing durable maternal lactogenic immunity for passive piglet protection.
<b>132</b>	Lin CM, Pathogenicity and immunogenicity of attenuated porcine epidemic diarrhea virus PC22A strain in conventional weaned pigs.	Review article	BMC veterinary research	none	NOT ABOUT CORONAVIRUS – 2 Therefore, P100C4 potentially could be tested as a priming vaccine or be further modified using reverse genetics. It also can be administered in multiple doses or be combined with inactivated or subunit vaccines and adjuvants as a PEDV vaccination regimen, whose efficacy can be tested in the future.



133	Alfaraj SH, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature.	Case reports and review	Journal of microbiology, immunology, and infection	2	NOT ABOUT CORONAVIRUS – 2 The overall case fatality rate remains high and is comparable to the overall case fatality rates. The disease had also resulted in fetal demise in 27% of cases.
134	Alfaraj SH, Middle East respiratory syndrome coronavirus in pediatrics: a report of seven cases from Saudi Arabia.	Case reports	Frontiers of medicine	7	NOT ABOUT CORONAVIRUS – 2 MERS-CoV remains an uncommon disease among children, and its course follows a milder path among children than those of adults. Majority of cases were asymptomatic and were diagnosed during the course of contact investigation.
135	Giersing BK, Report from the World Health Organization's third Product Development for Vaccines Advisory Committee (PDVAC) meeting, Geneva, 8-10th June 2016.	Special article: Report from WHO	Vaccine	none	NOT ABOUT CORONAVIRUS – 2

<b>136</b>	Andreeva A, Influence of interferon-based drugs on immunological indices in specific prevention.	Case-Control study	Veterinary world	45 cows	<b>NOT ABOUT CORONAVIRUS – 2</b> IFN-based drugs enhance the protective effect of vaccination against associative infections in the newborn calves. They stimulate a rise in the titer of antibodies to Rotavirus, coronavirus, VD, and mucosal disease complex as well as an increase in immunoglobulins A, M, and G.
------------	--	--------------------	------------------	---------	---