

## REVIEW PAPER

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# The novel coronavirus conundrum, the pregnant woman, her child What the obstetrician-gynecologist is learning La incógnita del nuevo coronavirus, la gestante y su niño Lo que el ginecobstetra está conociendo

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### ABSTRACT

The world has changed in the last few months with the appearance of a potentially severe viral disease denominated coronavirus disease 2019 – COVID 19. Initially confused with influenza because of its similar symptoms, it can lead to severe multiorgan complications including acute, deadly pneumonia and damage to the heart, kidneys, liver, bowel, coagulation and nervous system function. The incubation period is 5 to 7 days (range 2 to 14 days); it is more frequent in persons 30 to 79 years old, and less in people under 20. Lethality is about 5% (95% CI 0.5-15%). In this paper, we summarize what is known about its clinical presentation and recommendations from the American College of Obstetricians and Gynecologists, the Royal College of Obstetricians & Gynecologists, the Ministry of Health of Spain and specialized medical institutions and leading journals, on coronavirus disease-19 presentation, prevention and management in pregnant women and their newborns.

**Key words:** Pregnant women, Infant, newborn, Coronavirus 2019-nCoV – COVID 19.

### RESUMEN

El mundo ha cambiado en los últimos meses con la aparición de una enfermedad viral potencialmente severa viral denominada enfermedad por coronavirus 2019 – COVID 19. Inicialmente se la confundió con la influenza debido a síntomas similares, pero puede ocasionar complicaciones multiorgánicas severas como neumonía aguda mortal y dañar el corazón, los riñones, hígado, intestino, la coagulación sanguínea y la función del sistema nervioso. El periodo de incubación es de 5 a 7 días (rango 2 a 14 días), afectando principalmente a personas entre 30 y 79 años de edad, y con menos frecuencia por debajo de los 20 años de edad. La letalidad es alrededor de 5% (CI95% 0,5 a 15%). En el presente artículo se tratará de resumir lo que se conoce sobre su presentación clínica, y las recomendaciones del Colegio Americano de Obstetras y Ginecólogos, el Real Colegio de Obstetras y Ginecólogos, el Ministerio de Salud del Gobierno Español, y de instituciones médicas y revistas líderes especializadas, acerca de su presentación, prevención y manejo en las gestantes y recién nacidos.

**Palabras clave.** Gestantes, Recién nacido, Coronavirus 2019-nCoV – COVID 19.

### THE DISEASE

A potentially severe viral respiratory disease has suddenly appeared and disrupted the life of persons around the world in the past months. The disease has been denominated COVID-19 (coronavirus disease 2019), and is caused by the coronavirus SARS-CoV-2 (betacoronavirus, ssRNA). Other human coronavirus (HCoV) infections include HCoV 229E, NL63, OC43 and HKU1, which usually cause mild to moderate upper-respiratory tract illnesses like the common cold, Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). Initially, its symptoms were confused with influenza, as both present fever, sore throat, fatigue, loss of appetite, muscular and joint pain; however, this disease can lead to severe complications. On 31 December 2019, the disease was first reported in Wuhan City, Hubei Province, China, in 27 cases of severe viral pneumonia of unknown origin leading to acute respiratory distress. SARS-CoV-2 was identified in China as an emergent coronavirus on 7 January 2020. This virus has been evolving rapidly, with growing global case counts and



deaths every day in almost all countries around the world in only four months. Since January 2020, the virus might have been spreading in the U.S.A. The World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of international concern on 30 January 2020, and soon afterwards acknowledged the coronavirus as a pandemic on 11 March 2020. In Peru, the first case was detected on 5 March 2020<sup>(1)</sup>. As of 6 June 2020, 188 countries/regions around the world have reported a total of 6.761.942 confirmed cases and a death toll of 395.409 deaths<sup>(2)</sup>. Meanwhile, there are 187.400 confirmed cases and 5.162 deaths as of June 6 in Peru, overwhelming our health system. Two thirds of deaths occurred in elderly people, and so far, there are 1 435 physicians infected, and 51 deceased<sup>(3)</sup>. The disease seems to be slowing down in some countries.

## EPIDEMIOLOGY AND TRANSMISSION

The coronavirus SARS-CoV-2 is transmitted person-to-person via close contact with respiratory droplets produced when a person exhales, sneezes, or coughs; via direct contact with infected people; or via contact with fomites. Microdroplets (aerosols) may remain in the air for up to three hours<sup>(4)</sup>. It is also disseminated by mouth, nose and eye mucosa, touching one's face with hands, shaking hands, embracing, kissing, and touching contaminated objects, foods and clothing. The virus has been detected in blood, cerebrospinal fluid, saliva, tears, semen, and conjunctival secretions. Fecal-oral transmission may be possible<sup>(4)</sup>. Nosocomial transmission in healthcare workers and patients has been reported, as well as widespread transmission in long-term care facilities and on cruise ships.

The virus has been found to be more stable on plastic and stainless steel (up to 72 hours) compared with copper (up to 4 hours) and cardboard (up to 24 hours). Scientists in China have found that an infected person can appear asymptomatic for more than two full days while spewing contaminated secretions into the air, leaving the virus on doorknobs and handrails, silently sowing the seeds for future infections<sup>(4)</sup>.

Some people can be contagious during the incubation period; this period has been estimated to last between 1 and 14 days, with a median of 5

to 7 days (possibly longer in children). Coronavirus affects persons 30 to 79 years old and is less frequent among people under 20.

There is evidence that spread from asymptomatic carriers, about 30% of all the infected in the US, is possible. The proportion of asymptomatic cases in children is thought to be significant. In the USS Theodore Roosevelt aircraft carrier, 600 out of the 4 800-member crew tested positive for COVID-19, and 60% of them were asymptomatic. People might be most infectious with this novel disease before presenting any symptoms<sup>(5)</sup>.

## CLINICAL PRESENTATION

The clinical presentation of COVID-19 is that of a respiratory infection with symptom severity ranging from a mild common cold-like illness to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. COVID-19 disease is characterized by mild respiratory symptoms in about 85% of cases<sup>(6)</sup>. Non-specific symptoms may appear 2 to 14 days after exposure to the virus and include fever, respiratory symptoms (cough with or without sputum production, shortness of breath, or sore throat), muscle pain, fatigue, anosmia, ageusia, anorexia, malaise, nasal congestion, chills, headache, rash and, rarely, diarrhea, nausea and vomiting. Severe symptoms develop in 15% of cases, mainly in vulnerable persons over 60 years old or in people suffering from chronic diseases (heart disease, hypertension, obesity, lung disease, diabetes) and/or immunosuppression<sup>(7-9)</sup>. Coronavirus can damage the lungs, brain, eyes, nose, heart and blood vessels, kidneys, liver, intestine, and cause neurological malfunction<sup>(10,11)</sup>. Disease severity would depend on the SARS-CoV2 receptor angiotensin I-converting enzyme 2 (ACE2) amount found on the surface of cells throughout the body, including bowels, lungs, heart, nose. The increased number of ACE2 receptors correlates with higher risk of severe coronavirus infection. This would be a gene-dependent phenomenon. Lethality has increased from about 2% (95% CI 0.5-4%)<sup>(12)</sup> to 5% (0.5-15%)<sup>(13)</sup>. Infection in children is reported less frequently than among adults, in about 1 to 5%<sup>(4)</sup>. The term 'COVID toes' refers to a reddish-blue discoloration of the extremities prevalent in kids with critical COVID-19.



Regarding the experience of pregnant women with COVID-19 in Wuhan, China, the median age was 31 years, 52% were nulliparous, and 64% were infected with SARS-CoV-2 in the third trimester. The most common symptoms were fever (in 75%) and cough (in 73%); lymphopenia was present in 44% of patients, and 79% of women who underwent chest tomography had infiltrates in both lungs<sup>(14)</sup>. Compared with the risk of severe disease in the general population across mainland China (15.7%), the risk of severe disease was lower in pregnant women (8%). No positive results were reported in neonatal throat swabs of 8 newborns and breast milk samples from 3 mothers.

Besides patient age, preexistent chronic diseases, immunosuppression and lifestyle, it is possible that genetic and immune response variants are associated with vulnerability or resistance to coronavirus.

Secondary hemophagocytic lymphohistiocytosis (sHLH) is an under-recognized, hyperinflammatory syndrome characterized by fulminant and fatal hypercytokinemia ("cytokine storm") with multiorgan failure; cardinal features include unremitting fever, cytopenia, and hyperferritinemia, as well as pulmonary involvement<sup>(15)</sup>. In addition to respiratory compromise, cardiovascular complications are rapidly emerging as a key threat in COVID-19. SARS-CoV-2 infects the host using the ACE2 receptor, which is expressed in virtually all organs, including lung, heart, kidney, skin, stomach, small intestine, colon, bone marrow and brain. ACE2 receptors are also expressed by endothelial cells. In a series of patients with COVID-19, endothelial cell involvement across vascular beds of different organs has been shown<sup>(16)</sup>.

## PREVENTION AND TREATMENT

General prevention measures include: avoiding exposure to the virus, washing hands often with soap and water for at least 20 seconds or with a 60% alcohol-based sanitizer, avoiding coughing or sneezing and touching the eyes, nose, and mouth with unwashed hands, avoiding contact with people (distance over 2 meters), and shaking hands. If symptoms appear, seek medical care early; stay at home, clean and disinfect frequently touched surfaces<sup>(4)</sup>. Wear face masks especially in public settings where social distanc-

ing measures are difficult to maintain. Isolate all suspected and confirmed cases, implement recommended infection prevention and control procedures, and report all cases to local health authorities.

South Korea has successfully contained the advance of COVID-19 and flattened the curve of newly confirmed cases and deaths around mid-March. They have extensively used the country's advanced information technology system for tracing individuals suspected to be infected or who had been in contact with an infected person. As of 21 April 2020, there had been 10 683 confirmed cases in South Korea, with a total of 2 233 patients in isolation because of hospitalization or quarantine, and 237 deaths<sup>(17)</sup>. The same day, the U.S.A. reported 842 376 confirmed cases and 47 537 deaths, and Peru, 19 250 confirmed cases and 530 deaths. According to a Financial Times analysis of mortality data updated to 26 April 2020, the global coronavirus death toll could be 60% higher than reported, as mortality statistics show an excess of 122 000 deaths in global mortality rates across 14 countries. This was considerably higher than the 77 000 official COVID-19 deaths reported for the same places and time periods between 2015 and 2019<sup>(18)</sup>.

Currently, there is no specific treatment for COVID-19. Management of a patient with coronavirus is overall symptomatic. Recovered coronavirus patients may have a residual cough or fatigue and reduced lung function. Considering the fact that SARS-CoV-2 was detected in the semen of recovering patients, abstinence or condom use might be considered as preventive means for these patients<sup>(19)</sup>.

COVID-19 is here to stay. We do not know what its future behavior will be. Physicians, epidemiologists, scientists, statisticians and politicians are trying to predict the evolution of the disease by drawing curves of different sizes and inclinations to estimate the number of infected persons, those needing hospitalization, number of hospital beds in intensive care units, respirators and deceased persons. Governments approach flattening these curves through containment strategies to decrease the incidence of infected persons along with the number of hospitalizations, ICUs, respirators and cremations. On the other hand, the World Health Organization (WHO) informs there is currently no evidence of protec-



tion from a second infection in people who have recovered from COVID-19 and have antibodies against it<sup>(20)</sup>. Levels of antibodies against SARS-CoV-2 vary widely in patients after recovery; a proportion of them would recover without developing high titers of virus-specific neutralizing antibodies. These patients would be at risk of re-infection<sup>(21)</sup>. Some recovered patients may still be virus carriers, and potentially infectious. Current criteria for hospital discharge or discontinuation of quarantine and continuity of care may need to be reevaluated<sup>(22)</sup>. In South Korea, it has been reported that 260 patients thought to have recovered from the disease have tested positive again. Rather than viral reactivation or patient reinfection, the likely cause of positive results for SARS-CoV-2 would be fragments of dead viruses, days and even weeks after full recoveries<sup>(23)</sup>.

No coronavirus vaccine has ever been produced for coronavirus-19<sup>(24)</sup>, but we expect that one will be produced, hopefully soon, by Oxford University researchers and others.

We have realized we are dealing with an unknown viral disease, and we are not prepared for this type of crisis.

In the following lines, we would like to summarize the recommendations of important medical institutions and journals related to the practice of gynecology and obstetrics that will help to make decisions about women's care.

### **GYNECOLOGIC PATIENTS AND COVID-19**

The American College of Obstetricians and Gynecologists (ACOG) advises that determining the best management options for patients in the COVID-19 pandemic depends on the patient's signs and symptoms, their comorbidities and underlying medical condition, type of presentation (acute versus chronic) and available health resources, along with other factors<sup>(25)</sup>. Preventive visits, routine screenings, contraceptive counseling and prescribing, asymptomatic ovarian cyst, menopausal symptoms, routine gynecologic or postoperative follow-up, mental or behavioral health screening may be addressed by telehealth or deferred until after the COVID-19 outbreak<sup>(25)</sup>.

A remote approach via phone calls can be considered for the routine screening of patients for potential exposure to COVID-19, asking about recent travel history, potential exposure and symptoms. If infection is suspected, the patient will be counseled to go to a local health institution for management of coronavirus. Limitations to the number of persons accompanying the patient should be based on local institutional or practice recommendations, as well as patient's need.

Confidentiality is a vital component of the patient-gynecologist relationship, especially for adolescent patients or patients at high risk of intimate partner violence.

Elective surgeries should be postponed; however, obstetric and gynecologic procedures for which a delay would negatively affect patient health and safety should not be delayed<sup>(25)</sup>.

### **PREGNANT WOMEN DURING THE COVID-19 PANDEMIC**

Very little is known about COVID-19 and its effect on pregnant women and infants; currently, there are no specific recommendations regarding the evaluation or management of COVID-19<sup>(26)</sup>.

The available evidence to guide coronavirus clinical management is of low quality –level 3 or 4, or grade D<sup>(27)</sup>. Limited data do not indicate a higher risk of infection or severe morbidity in pregnant women. Pregnancy itself alters the body's immune system and response to viral infections in general, which can occasionally cause more severe symptoms. Pregnant patients with comorbidities may be at a higher risk for severe illness, consistent with the general population with similar comorbidities<sup>(27)</sup>.

Hospitals that provide maternity services should create or—if already established—activate their perinatal subcommittee in charge of disaster preparedness (likely to include representatives from obstetric, pediatric, family medicine, and anesthesia teams, among others)<sup>(26)</sup>. Regardless of whether an area is currently experiencing wide community spread, the ACOG encourages all facilities to strategize how to expand their obstetric work force.



Obstetrician-gynecologists and the entire maternity care team are committed to ensuring that pregnant patients or those considering becoming pregnant have the patient-centered, safe care they need. Should a patient decide to pursue pregnancy, prepregnancy counseling can be initiated through telehealth. Spacing out, reducing prenatal appointments or, when appropriate, providing care through telehealth, may mitigate some of the strain on resources and reduce the risk of inadvertent exposure to COVID-19<sup>(26)</sup>. Electronic record systems should be used. When seeing patients face-to-face, simultaneous electronic documentation will facilitate future remote consultation<sup>(27)</sup>.

Pregnant women are in the vulnerable category, so they are advised to follow strict social distancing measures and stay-at-home orders, particularly if they are above 28 weeks' gestation. Remote consultations and self-monitoring of blood pressure may be recommended in healthy women whenever possible to reduce the number of hospital visits. Requests for leave will depend on the patient's comorbidities and individual work situation. Remote follow-ups for monitoring diabetes, hypertension, mood disorders and other conditions should be considered<sup>(27)</sup>.

Routine antenatal care appointments should be delayed in patients with suspected or confirmed COVID-19 until after the recommended period of self-isolation. Appointments can be deferred until 7 days after the start of symptoms, unless they worsen. For women who are self-isolating because someone in their household is under suspicion of COVID-19, appointments should be deferred for 14 days<sup>(27)</sup>. More urgent appointments require a senior decision on urgency and potential risks and benefits.

When possible, antenatal fetal surveillance and ultrasonography should continue as medically indicated. Elective ultrasound examinations should not be performed. A detailed mid-trimester anatomy ultrasound examination may be considered following first-trimester maternal infection with COVID-19<sup>(4)</sup>.

Following delivery and in order to limit the risk of inadvertent exposure and infection, it may be appropriate to expedite discharge when mother and infant are healthy; this should be linked to home telehealth visits for both<sup>(27)</sup>. Maternity services should offer a combination of face-to-face

and remote postnatal follow-up, according to the needs of mother and newborn, for example in cases of hypertensive diseases of pregnancy, low birth weight, prematurity or if there are any concerns about feeding.

## PREGNANT WOMEN WITH COVID-19

Data on pregnant women with COVID-19 are limited. No specific treatments are known to be effective for COVID-19 yet. The mainstay of management is early recognition and optimized supportive care<sup>(4)</sup>.

The ACOG has published an algorithm to help decide whether hospital admission or home care is more appropriate<sup>(28)</sup>.

Retrospective reviews of pregnant women with COVID-19 found that they appeared to have fewer adverse maternal and neonatal complications and outcomes than those expected with severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS)<sup>(4)</sup>. However, pregnancy seems to have worsened the course of COVID-19 in Spanish patients, with longer hospital stay, higher rate of renal failure, sepsis, disseminated intravascular coagulation, intensive care unit use, mechanical ventilation and higher lethality<sup>(12)</sup>.

The clinical characteristics of pregnant women with COVID-19 are similar to those reported in non-pregnant adults. Symptoms due to physiological adaptations of pregnancy or adverse pregnancy events (e.g., dyspnea, fever, gastrointestinal symptoms, fatigue) may overlap with COVID-19 symptoms<sup>(4)</sup>. Miscarriage (2%), intrauterine growth restriction (10%), and preterm birth (39%) have been reported, but it is unclear whether this is related to COVID-19. There is one published case of stillbirth in a woman with severe COVID-19 at 34 weeks gestation<sup>(27)</sup>.

Patients should be managed in a hospital setting when possible; however, home care may be suitable for selected patients with mild illness unless there is concern about rapid deterioration or an inability to promptly return to the hospital if necessary. Patients should remain in isolation for 2 weeks after symptoms disappear, and visitors should not be allowed until the end of this period<sup>(4)</sup>. Pregnant women should be managed by a multidisciplinary team, including obstetric,



perinatal, neonatal, and intensive care specialists, as well as mental health and psychosocial support<sup>(4)</sup>. Teach patients to seek medical help immediately if they have trouble breathing, if their lips or face turn blue, if they have persistent chest pressure or pain, or if they are confused or unable to get out of bed.

Regarding infection prevention and control in inpatient obstetric care settings, health care practitioners should promptly notify infection control personnel at their facility of the anticipated arrival of pregnant patients with confirmed COVID-19 or under investigation<sup>(29)</sup>.

Manage suspected and confirmed cases with appropriate maternal and fetal monitoring whenever possible. Women with severe illness or complications may require admission to an intensive care unit. Consider home care in women with asymptomatic or mild illness, provided that the patient is able to care for herself, that monitoring and follow-up are possible and that the patient has no signs of potentially severe illness (e.g. breathlessness, hemoptysis, new chest pain or pressure, anorexia, dehydration, confusion), no comorbidities and no obstetric issues<sup>(27)</sup>.

Samples required for an initial nucleic acid test in a pregnant woman with COVID-19 are a single swab used for throat and nose (nasopharyngeal secretions), and sputum, if available<sup>(30)</sup>. In addition, testing specimens from multiple sites like blood, feces, urine and conjunctival secretions may increase sensitivity and reduce false-negative test results<sup>(31)</sup>. Samples should be processed in an appropriate laboratory.

Perform a nucleic acid amplification test, such as real-time reverse-transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2, in patients with suspected infection, confirming by nucleic acid sequencing when necessary<sup>(4)</sup>. Results from RT-PCR suggest that high viral loads may be detected soon after illness onset, including in minimally symptomatic persons<sup>(32)</sup>. One or more negative results do not rule out the possibility of infection. The tests may come back with false positives, false negatives or confoundingly ambiguous results. Remember that improper sampling accounts for some false negative results. Collect nasopharyngeal swabs for testing to rule out infection with other respiratory pathogens (e.g., influenza, atypical pathogens), as co-infections can occur.

Specific antibodies are produced after SARS-CoV-2 infection. Positive serum-specific IgM or specific IgG antibody titer in the recovery phase approximately 4 times higher than that in the acute phase can be used as diagnostic criteria for suspected patients with negative nucleic acid tests. During follow-up, IgM is detectable 10 days after symptom onset and IgG is detectable 12 days after symptom onset. The viral load gradually decreases as serum antibody levels increase<sup>(33)</sup>. Many people with COVID-19 are asymptomatic, and widespread testing of SARS-CoV-2 specific antibodies would provide insights into how prevalent the most serious cases have been. Also, if a large percentage of people in a city or country have those antibodies, researchers might determine there is enough herd immunity to protect those who haven't contracted the virus yet.

Lung ultrasound may be a clinically useful tool in assessing pulmonary compromise. Chest imaging and CT scan are considered safe in pregnant women. Multiple bilateral lobular and subsegmental areas of ground-glass opacity or consolidation are seen in most patients, usually with a peripheral or posterior distribution, mainly in the lower lobes and less frequently in the right lower lobe. Crazy-paving pattern, air bronchograms, reversed halo sign and perilobular pattern, in other words, patterns of organizing pneumonia, may also appear<sup>(4)</sup>. Abnormalities can rapidly evolve from focal unilateral to diffuse bilateral ground-glass opacities that progress to or co-exist with consolidations within 1 to 3 weeks.

Treatment for severe COVID-19 include admission to critical care, prone position, appropriate monitoring and supportive therapies such as oxygen and airway management, fluids, prevention of complications (acute respiratory distress syndrome (ARDS), sepsis, and septic shock), antimicrobials within 1 hour of initial patient assessment for suspected sepsis, and management following institutional guidelines of fever (consider paracetamol), cough and breathlessness, anxiety, delirium, and agitation. Consider intubation and mechanical ventilation in patients who are acutely deteriorating. Pregnant women may benefit from lying in the lateral decubitus position<sup>(4)</sup>.



Critical illness increases in later pregnancy compared with early pregnancy, with a heightened risk of indicated preterm birth<sup>(34)</sup>. Corticosteroid therapy may be considered in women who are at risk of preterm birth from 24 to 37 weeks gestation for fetal lung maturation. Although it was acknowledged that corticosteroids could potentially worsen the maternal condition, they are currently used as an anti-inflammatory.

Choice of delivery and timing should be individualized based on gestational age, as well as maternal, fetal and delivery conditions. Induction of labor and vaginal delivery is preferred in pregnant women with confirmed COVID-19 infection to avoid unnecessary surgical complications; however, emergency cesarean delivery may be required if medically justified (e.g., maternal sepsis or fetal distress). If possible, a negative pressure isolation room is recommended for labor, delivery and neonatal care in confirmed cases<sup>(27)</sup>.

Following delivery, families should be provided with guidance about how to identify signs of illness in their newborn or worsening of the woman's symptoms, as well as with appropriate contact details if they have concerns or questions about their baby's wellbeing. All families are recommended to self-isolate at home for 14 days after birth of a baby to a woman with active COVID-19 infection<sup>(27)</sup>.

More on specialized care of patients with severe disease can be found in the recent and ample literature available.

### PLANNING DELIVERY IN PATIENTS WITH CORONAVIRUS-19

The New England Journal of Medicine (NEJM) has published the following suggestion from the Columbia University Irving Medical Center, after their experience with pregnant women hospitalized for delivery in this pandemic: use universal SARS-CoV-2 testing in all pregnant patients presenting for delivery because most patients positive for SARS-CoV-2 at delivery were asymptomatic, and over one in eight asymptomatic patients admitted to the labor and delivery unit were positive for the virus. This would help to determine hospital isolation practices and bed assignments, inform neonatal care, and guide the use of personal protective equipment<sup>(35)</sup>.

In patients under 24 weeks pregnant with COVID-19 infection, fetal viability should be checked and then the same procedure for the general population should be followed. In women 24 weeks pregnant or more, fetal wellbeing will be established and the patient will remain in observation awaiting the diagnostic test results. Ultrasound examination and cardiotocography will be performed according to weeks of pregnancy<sup>(12)</sup>.

When a pregnant patient with suspected or confirmed COVID-19 is admitted and birth is anticipated, the obstetrician, midwife-in-charge, neonatologist, neonatal nurse, pediatric or family medicine and anesthesia teams should be notified in order to facilitate care. All staff should have been trained in the use of personal protective equipment (PPE) so that 24-hour emergency theatres are available and possible delays reduced. Women should be allowed and encouraged to have an asymptomatic birth partner with them during labor and delivery, unless the birth occurs under general anesthesia<sup>(27)</sup>. Many hospitals are banning partners from births during coronavirus pandemic. Efforts should be made to minimize the number of staff members entering the room and units.

In most cases, timing of delivery should not be dictated by maternal COVID-19 infection. For women with suspected or confirmed COVID-19 early in pregnancy who have recovered, no alteration to the usual timing of delivery is indicated. For women with suspected or confirmed COVID-19 in the third trimester who have recovered, it is reasonable to attempt to postpone delivery (if no other medical indications arise) until a negative testing result is obtained or quarantine status is lifted, in an attempt to avoid transmission to the neonate<sup>(26)</sup>. Inductions of labor and cesarean deliveries should continue to be performed as indicated. Due to the possibility of fetal compromise, continuous electronic fetal monitoring in labor is currently recommended for all women with COVID-19<sup>(27)</sup>. Fever should be investigated and treated accordingly. Vaginal secretions tested for COVID-19 have yielded negative results<sup>(27)</sup>.

### DELIVERY IN PATIENTS WITH CORONAVIRUS-19

All women should be encouraged to call the maternity unit for advice in early labor. Women with mild COVID-19 symptoms can be encouraged to



remain at home (self-isolating) in early labor. They should be advised to attend an obstetric unit for birth, where the baby can be under continuous electronic fetal monitoring<sup>(12)</sup>.

Mode of birth should be discussed with the pregnant woman, considering gestational age, her preferences and medical, obstetric or pediatric indications for intervention. This decision should not be influenced by the presence of COVID-19, unless the woman's respiratory condition demands urgent intervention for birth. Consider personal protective equipment for labor including cap, glasses, waterproof boots, gloves and FFP2 surgical masks<sup>(12,27)</sup>. It is suggested to attend vaginal deliveries in the patient's conditioned room or in a special delivery room for COVID-19 infected people.

Management of labor is not altered in women giving birth during the COVID-19 pandemic or in women with confirmed or suspected COVID-19. Labor, and particularly pushing, often causes loss of feces, where the virus can be present and spread the infection<sup>(36)</sup>.

Elective instrumental birth may be considered in a symptomatic woman who is becoming exhausted or hypoxic<sup>(27)</sup>. Cesarean delivery should be based on obstetric (fetal or maternal) indications and not on COVID-19 status alone. Epidural analgesia may be recommended in labor to women with suspected or confirmed COVID-19, to minimize the need for general anesthesia if urgent intervention for birth is required.

Current evidence-based guidelines for delayed cord clamping should continue to be followed. If an adequate mother-child isolation is warranted, skin to skin contact after birth could be possible<sup>(12)</sup>.

It may be appropriate to temporarily consider tubal sterilization only when performing cesarean birth (unless she is a high risk patient) and, as long as an alternative form of contraception is provided, consider it otherwise elective<sup>(27)</sup>.

Pregnant women with severe illness should be monitored with pulse oximetry, arterial blood gas analysis, full blood count, comprehensive metabolic panel, coagulation screen, inflammatory markers (serum procalcitonin and C-reactive protein), serum troponin, serum lactate de-

hydrogenase and serum creatine kinase. These patients can present leukopenia, lymphopenia, leukocytosis, elevated liver transaminases, elevated lactate dehydrogenase and elevated C-reactive protein, neutrophilia, thrombocytopenia, decreased hemoglobin, decreased albumin, renal impairment, and low oxygen saturation<sup>(4)</sup>.

There have been case reports of women with severe COVID-19 at the time of birth who required ventilation and extracorporeal membrane oxygenation<sup>(37)</sup>. In the United Kingdom, the rate of current/recent pregnancy among all individuals admitted to critical care (2.3%) remains similar to the reported rate for non-COVID viral pneumonia from 2017 to 19 (3.3%)<sup>(27)</sup>. Emerging evidence suggests that individuals with COVID-19 admitted to a hospital are in a hypercoagulable state; since there is an increased risk of maternal venous thromboembolism (VTE), women should be assessed for this condition after birth<sup>(27)</sup>. For women receiving postpartum anticoagulation, the optimum duration of therapy is unclear. Some recommend discontinuing prophylaxis upon discharge, and others, to continue prophylaxis for up to 10 to 14 days. Patients at high risk of VTE receive a longer course, depending on the indication for prophylaxis<sup>(37)</sup>.

## THE FETUS

No current data suggest a higher risk of miscarriage or early pregnancy loss in relation to COVID-19, nor that the virus is teratogenic<sup>(27)</sup>. There are some case reports of preterm birth in women with COVID-19, which may in part be due to a medical indication. To date, there is no conclusive evidence of vertical transmission of COVID-19<sup>(26)</sup>, but COVID-19 placentas may have features of maternal vascular malperfusion. Emerging evidence now suggests that vertical transmission is probable<sup>(27)</sup>. Since IgM does not cross the placenta, findings of IgM in a fetus are likely due to a neonatal immune response to an *in-utero* infection.

## THE NEWBORN

There have been case reports of infection in neonates born to mothers with COVID-19, and virus-specific antibodies have also been detected in neonatal serum samples. It is unknown whether perinatal transmission (including transmission via breastfeeding) is possible. Horizontal





transmission is the same as for the general population. Severe disease in term newborns has not been reported. Amniotic fluid, cord blood and newborn throat swab from six mothers positive for COVID-19 were all negative by RT-PCR<sup>(38)</sup>.

Adverse effects reported in newborns include fetal distress, prematurity, respiratory distress, thrombocytopenia, non-significant leukopenia and mild increase of liver function tests; however, it is unclear whether these effects are related to maternal SARS-CoV-2 infection.

The clinical symptoms from 33 neonates born to mothers with COVID-19 in Wuhan, China, were mild, and outcomes were favorable. Among the neonates with symptomatic COVID-19, the most seriously ill case may have been due to prematurity, asphyxia, and sepsis, rather than SARS-CoV-2 infection<sup>(39)</sup>.

Babies born to mothers with suspected or confirmed infection should be considered a person under investigation (PUI) and tested at 24 hours and 48 hours after birth. The WHO recommends that mothers and infants should remain together when possible, and breastfeeding should be encouraged while applying appropriate infection prevention and control measures (e.g., hand hygiene before and after contact with the baby, wearing a mask while breastfeeding). However, the CDC recommends that temporary separation of mother and baby should be considered on a case-by-case basis, at least until the mother's transmission-based precautions are discontinued. Separation appears to be the best option for mothers who are severely or critically ill<sup>(4)</sup>.

After discharge, advise mothers with COVID-19 to practice prevention measures (e.g., distance, hand hygiene, respiratory hygiene/mask) for newborn care until they are afebrile for 72 hours without using antipyretics and until at least 7 days have passed since symptoms first appeared. A newborn with documented infection requires close outpatient follow-up after discharge<sup>(4)</sup>.

## BREASTFEEDING

In limited case series reported to date, the virus has not been detected in the breast milk of women infected with COVID-19; however, it is not yet known if COVID-19 can be transmitted through breast milk<sup>(29)</sup>.

There are rare exceptions when breastfeeding or feeding expressed breast milk are not recommended. The mother, in coordination with her family and health care practitioners, should make the decisions about starting or continuing breastfeeding and how to do so. Currently, the primary concern is not whether the virus can be transmitted through breast milk, but rather whether an infected mother can transmit the virus through respiratory droplets during breastfeeding.

A mother with confirmed COVID-19 or who is a symptomatic PUI should take all possible precautions to avoid spreading the virus to her infant, including washing her hands before touching them and wearing a face mask while breastfeeding. If expressing breast milk with a manual or electric breast pump, the mother should wash her hands before touching any pump or bottle parts and follow recommendations for proper pump cleaning after every use. If possible, consider having someone without disease feed the expressed breast milk to the infant<sup>(29)</sup>.

Kangaroo mother care must follow all safety protocols for COVID-19. Provide oral colostrum care to all hospitalized newborns and limit feeding with substitutes unless medically justified<sup>(38)</sup>.

## THE IMMEDIATE FUTURE

We hope we will have antiviral treatment and a vaccine within this or next year. There is great expectation regarding the safety and outcomes of Remdesivir antiviral drug therapy, a novel nucleotide analogue that has shown in vitro activity against SARS-CoV-2 and related coronaviruses<sup>(37)</sup>.

Ongoing clinical trials and investigations seek to learn more about the virus, its origin, and how it affects humans. Experience calls for a big data collection and analysis effort to address the many unanswered questions about the virus. Meanwhile, in developing countries, the COVID-19 curve is not flattening as we were promised it would.

Three steps to ending the COVID-19 lockdown include the strategy of massive scale testing, prompt contact tracing, and quarantine and isolation. This should include women considering becoming pregnant or already pregnant. When



the curve slows down, mitigation strategies rely on nonpharmaceutical interventions such as hand hygiene, travel restrictions, school closures, and social distancing. In this scenario, the spread of the virus slows and hospitals are less overburdened<sup>(40)</sup>.

In the absence of a vaccine, recurrent outbreaks of disease are expected, with increases in hospitalizations and busy mortuaries. Epidemiologists expect resurgent waves of infection that could last into 2022. Women should wear masks and apply social distancing, and consider postponing pregnancy in some geographic areas. Testing must be accessible to anyone with any symptom suggestive of COVID-19, including health care workers, teachers, service industry employees, athletes. Contacts of people with COVID-19 should be properly identified. Serologic testing for SARS-CoV-2-specific IgM and IgG immunoglobulins will provide estimates of population exposure. Crowding must be limited (festivals, conferences, large gatherings, sporting events, office, malls, stores and restaurants). Vulnerable populations in our region should be addressed with both social justice and the development of a comprehensive public health plan, needs that currently do not exist<sup>(40)</sup>.

Hospital medical teams and mortuary workers in many parts of the world are overwhelmed. Epidemiologists say that the true lethality of the virus is almost certainly overestimated in fatality rates that are based on comparing deaths, which are relatively easy to count, to infections, which are not. In cooperation with health officials, they have estimated that, in some communities, for every confirmed case, there are five to ten people with undetected infection, and at least one estimate suggests there are far more. By 20 April 2020, California had 33 686 confirmed cases and 1 223 deaths, according to Los Angeles Timer Coronavirus Today. Preliminary results from the University of Southern California propose that the number of COVID-19 cases in Los Angeles County may be more than 50 times greater than the official count. The study estimates that as many as 442 000 adult residents, about 5 percent of Angelenos, may have already been infected with COVID-19. In Lima, Peru, by 27 April 2020, there were officially 358 COVID-19 deaths. However, compared with tendencies from 2017-2019, the number of expected deaths surpassed the official account of deaths by 1850<sup>(41)</sup>.

Mental stress and mental disorders in people have more than doubled. And hospitals prepare for wave of mental health disorders including anxiety, depression or post-traumatic stress, confusion, and anger among their workers.

The four essential criteria outlined by epidemiologists to end the quarantine are<sup>(42)</sup>:

- The number of new cases must decline for at least two consecutive weeks.
- The government/state must be able to perform contact tracing on every new case that appears.
- Tests must be available to diagnose any person with symptoms.
- The healthcare system must have the capacity to treat all patients, not just those with COVID-19.

Are we ready?

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