

Fetal Diagnosis and Therapy during the COVID-19 Pandemic: Guidance on Behalf of the International Fetal Medicine and Surgery Society

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Keywords

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Abstract

The COVID-19 pandemic has stressed patients and health-care givers alike and challenged our practice of antenatal care, including fetal diagnosis and therapy. This document aims to review relevant recent information to allow us to optimize prenatal care delivery. We discuss potential modifications to obstetric management and fetal procedures in SARS-CoV2-negative and SARS-CoV2-positive patients with fetal anomalies or disorders. Most fetal therapies are time sensitive and cannot be delayed. If personnel and resources are available, we should continue to offer procedures of

proven benefit, acknowledging any fetal and maternal risks, including those to health care workers. There is, to date, minimal, unconfirmed evidence of spontaneous vertical transmission, though it may theoretically be increased with some procedures. Knowing a mother's preoperative SARS-CoV-2 status would enable us to avoid or defer certain procedures while she is contagious and to protect health care workers appropriately. Some fetal conditions may alternatively be managed neonatally. Counseling regarding fetal interventions which have a possibility of additional intra- or postoperative morbidity must be performed in the context of local resource availability. Procedures of unproven benefit should not be offered. We encourage participation in registries and trials that may help us to understand the impact of COVID-19 on pregnant women, their fetuses, and neonates.

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Introduction

The COVID-19 pandemic, caused by severe acute respiratory syndrome-corona virus-2 (SARS-CoV-2), has altered our delivery of medical care globally. Patient mobility is limited, health care services are overwhelmed, medical personnel are reallocated, and resources are depleted, leading to rapidly changing policies and management strategies. One consequence is an alteration in the care of pregnant women and their fetuses. Modification and downscaling of such care poses the risk of diagnostic and therapeutic fetal procedures being deferred and/or their use being queried [1–3]. Therefore, pregnant women may, in addition to their concerns about COVID-19, be anxious about not receiving optimal antenatal care. For some fetal conditions, this may mean that not all interventional options remain available.

The International Fetal Medicine and Surgery Society (IFMSS) wishes to complement the guidelines from authorities and professional organizations, specifically those pertaining to fetal medicine, while reconciling the fetal-maternal perspectives, healthcare workers' (HCW) health, and public interest. We aim to provide a comprehensive overview, acknowledging that this may quickly become outdated. The scientific knowledge and impact of this pandemic change daily. Any guidelines should therefore be reconciled with those from authorities in infectious disease, pediatric surgery, anesthesia and transfusion, critical care, and maternal-fetal medicine.

Fetal Diagnosis and Prenatal Screening in the COVID-19 Era

During this pandemic, individual preference should be weighed against the greater societal good. To ensure that our healthcare system is not overwhelmed, we should consider segregating teams by practice location, timing, and expertise [4]; nonessential services should be deferred or delayed and we must minimize contact between individual patients and HCW.

Several guidelines on amended care in pregnancy care, labor, and delivery in the COVID-19 era have already been published [1–10]. Antenatal visits can be spaced out [10] and telemedicine [11] and home-based care should be utilized whenever possible [6, 7, 10]. The first antenatal visit can be virtual, following a home pregnancy test, to identify risk factors that may be evident in the first trimester. Counselling for Down syndrome screening can be performed and consent obtained virtually. A 12- to 13-

week ultrasound (US) can be used to date the pregnancy, confirm viability, screen for multiples and chronicity, exclude major structural abnormalities, and assess nuchal translucency and, simultaneously, blood can be drawn for routine antenatal, biochemical, or noninvasive prenatal screening. Follow-up visits to discuss results can be virtual. Anatomical US should be delayed until 20–22 weeks to optimize their accurate completion.

Antenatal Care for Women with SARS-CoV-2 Infection

Some patients whose fetus has an anomaly or disorder will also have SARS-CoV-2 infection of varying severity. The effects of this infection on mothers and fetuses are currently unknown, and the effect of pregnancy on the clinical course of COVID-19 disease has not been accurately characterized [4]. It seems that pregnant women are not more prone to developing COVID-19, and their disease course is not worse. In up to 9% of pregnancies, the condition could be severe, but in >90% it will be mild [12–17]. Symptoms include pyrexia, sore throat, cough, anosmia, dyspnea, myalgia, and/or malaise, and more severe presentations range from pneumonia to acute respiratory distress syndrome and multiorgan failure [13, 14]. Presentations in pregnancy may be atypical, such as an absence of fever or leucocytosis [15]. When complications occur, these are predominantly preterm birth, preterm prelabour rupture of membranes, preeclampsia, cesarean delivery, and possibly intensive care unit (ICU) admission for ventilation or extracorporeal membrane oxygenation [18].

In the case of pregnant women testing positive for SARS-CoV-2 or COVID-19 disease, one would intuitively intensify maternal and fetal surveillance, but the potential benefits of such measures need to be balanced against the risks of viral transmission to HCW and other patients and the increased burden on already overstretched healthcare services.

– For asymptomatic or mildly symptomatic SARS-CoV-2-positive women, most fetal screening can safely be postponed until the infection has resolved. Asymptomatic [19] and presymptomatic [20] carriers can infect others, but their period of contagion is unknown [21, 22]. In most places a 14-day isolation period and being asymptomatic are used as guidelines. If the window of opportunity for US screening for trisomy 21 has passed, noninvasive prenatal screening is a reasonable alternative.

- SARS-CoV-2 infection in pregnancy may increase the risk of preterm birth or fetal growth restriction [4]. Therefore, some recommend US monitoring at 4-week intervals for growth, amniotic fluid volume, and umbilical artery Doppler as indicated [2, 4]. In medical or obstetric emergencies, appropriate intervention should be based on clinical expediency.
- The care of symptomatic COVID-19 pregnant women should be tailored to their specific symptoms with multidisciplinary input. Fetal wellbeing should be evaluated, as maternal respiratory insufficiency can lead to fetal compromise. Whenever possible, vaginal delivery is favoured to avoid unnecessary surgical complications in an already sick patient. Caesarean delivery should be performed based on standard obstetric indications, in cases of septic shock or acute organ failure, or to facilitate maternal ventilation or resuscitation, as this may improve the maternal condition [1, 2, 18]. Potential side effects of corticosteroids for fetal lung maturity in COVID-19 infection have been debated, partly based on observations that glucocorticoids increase viral replication in certain circumstances [23]. Corticosteroids should therefore not be used in asymptomatic SARS-CoV-2-positive patients or those with mild COVID-19 symptoms, unless preterm birth <34 + 0 weeks' gestation is anticipated [2, 24]. Their use in ICU patients should be judiciously evaluated, as well as in patients at >34 + 0 weeks' gestation [25].

There is currently little evidence of spontaneous vertical fetal transmission of SARS-CoV-2. This is somewhat counterintuitive given that the angiotensin-converting enzyme 2 viral receptor is widely expressed in the placenta [26, 27]. One possible explanation is that the placenta does not express transmembrane serine protease TMPRSS2, which also plays a role in cell entry for the SARS-CoV-2 virus, yet this is hypothetical [28, 29]. We are unaware of documented, spontaneous vertical transmission, though limited numbers have been reported to date [13, 30, 31]. In most cases, mothers infected in the third trimester deliver rapidly after symptom onset, thereby limiting the potential for in utero transmission. There are no reports (yet) of virus found in amniotic fluid or cord blood [13]. It is too early to determine whether spontaneous viral transmission earlier in pregnancy is more likely and/or has more adverse effects, but COVID-19 pregnancy outcome registries should help to clarify this. IgM antibodies were detected shortly after birth in the serum of 3 symptomatic neonates [32, 33], suggesting viral exposure in utero, but IgM-based assays can be falsely positive [34].

Fetal Procedures in COVID-19 Times

Most fetal therapies are time sensitive, and delaying them may worsen fetal, neonatal, and even maternal outcomes [35–38]. Fetal therapy should therefore not be defined as “elective.” Its provision should be guided by institutional policies and practices in the context of local resource availability. We present 3 considerations regarding fetal interventions with SARS-CoV-2 infection.

Risk of Vertical Transmission during Fetal Procedures

Any invasive procedure in a SARS-CoV-2-positive woman theoretically poses a risk of vertical transmission similar to that observed in HIV-positive women prior to effective antiviral therapy being available. There is no confirmed evidence that such vertical transmission occurs with COVID-19, so minimally invasive procedures (e.g., amniocentesis or fetoscopy) should continue to be offered, ideally avoiding transplacental passage, which increases the risk of intra-amniotic bleeding and disrupts the feto-maternal barrier. Similarly, amniocentesis may be preferable to chorionic villus sampling (Table 1). With open fetal surgery, the risk of maternal-fetal transmission is likely higher than that with needle or fetoscopic procedures as the fetus is exposed to maternal blood and its skin integrity is breached. We recommend postponing such interventions until maternal viral clearance has been documented.

Maternal Considerations

SARS-CoV-2-negative patients in whom fetal interventions are planned should be informed that additional assessments, hospital visits, and travel will increase their exposure to HCW and other patients and might increase their risk of infection. For international travel, additional restrictions may apply, and patients may find themselves temporarily “trapped” abroad. Patients should also be aware that COVID-19 infection might compromise their pregnancy outcome [4].

The risk of an asymptomatic SARS-CoV-2-positive pregnant woman progressing to mild or severe COVID-19 disease is unknown, but is usually thought to be equivalent to that of health- and age-matched women [10, 39]. Nevertheless, pregnancy's physiological changes may predispose to cardiorespiratory instability [4]. To avoid the coincidence of iatrogenic surgical morbidity with additional infection related-problems, it may be prudent – fetal condition allowing – to delay interventions until maternal infection has cleared. Typically, this is said to be around 2–3 weeks in asymptomatic women, though a

Table 1. Diagnostic and therapeutic procedures, estimated risks and benefits, and position based on the current knowledge and available resources

Procedure	Benefit to the fetus/mother	Theoretical risk of vertical transmission	Risk to healthcare provider	Maternal ICU need	Resource utilization	Recommendation
Chorionic villus sampling	high	moderate	low	unlikely	minimal	offer to screen negative patients; delay to amniocentesis in symptomatic and screen positive patients
Amniocentesis	high	low	low	unlikely	minimal	offer to asymptomatic patients; others: consider delay if possible
Fetal blood transfusion	high	moderate	low	unlikely	moderate	offer to screen negative patients; adjust for symptomatic patients or screen positive patients if it cannot be delayed
Fetal cardiac procedures	unknown	moderate	low	unlikely	moderate	consider not offering
Thoraco-amniotic shunting	high	moderate/high	low	unlikely	moderate	offer to screen negative patients, adjust for symptomatic patients or screen positive patients if it cannot be delayed
Vesico-amniotic shunting	low	moderate/high	low	unlikely	moderate	consider not offering screening
Fetal cystoscopy	unknown	moderate/high	low	unlikely	moderate	consider not offering screening
Laser for TTTS	high	low	low	unlikely	moderate	offer to screen asymptomatic patients; adjust for symptomatic patients or screen positive patients if it cannot be delayed
Selective feticide in mono chorionic twins	variable	low	low	Unlikely	moderate	offer to screen asymptomatic patients; adjust for others
Tracheal occlusion for CDH	unknown	low	low	unlikely	moderate	consider not offering screening
Spina bifida closure	high	high	moderate/high	low	high	delay if gestational age allows; if not, offer only to screen negative patients if sufficient local resources are available.

Rare conditions and procedures will need to be discussed on a case-by-case basis. Reproduced from Deprest et al. [1] and reprinted with permission. TTTS, twin-to-twin transfusion syndrome; CDH, congenital diaphragmatic hernia.

longer shedding period has been described. Additionally or alternatively – resources allowing – one could await 2 consecutive negative swabs.

For procedures requiring general endotracheal anesthesia (GA), which carries a higher risk of aerosolized viral transmission, one may need to be more restrictive. Even asymptomatic patients operated upon electively in the incubation period are at an increased risk [40].

For symptomatic SARS-CoV-2-positive women (hence with COVID-19), it is preferable to delay fetal interventions whenever possible, firstly because COVID-19 symptoms of coughing and dyspnea may interfere with surgery and secondly because surgical stress may trigger COVID-19 deterioration or iatrogenic complications [41]. A relevant example is prenatal spina bifida repair, which is always performed under GA and carries an increased risk of postoperative respiratory problems, which

could be mitigated by not using MgSO₄. Delaying fetal surgery, or even postponing repair until after birth, if it cannot be done within the optimal gestational age window, seems more prudent. Fetal benefits seem to decrease with advancing gestation; there is no evidence that prenatal spina bifida repair after 26 weeks improves outcomes [42].

Life-Saving Fetal Therapies

Life-saving fetal therapies usually performed under local anesthesia and conscious sedation should continue as maternal morbidity is low with this mode of anesthesia [41]. This includes fetoscopic placental laser ablation for twin-twin transfusion syndrome. In twin-twin transfusion syndrome, postponing intervention may lead to fetal death, preterm birth, or maternal complications, such as abruptio; amnioreduction will also facilitate maternal respira-

tion. Fetal transfusions and shunting for fetal hydrops due to pleural effusions or macrocystic lung lesions should likewise continue (Table 1). Investigational procedures or fetal interventions of unproven benefit should not be performed.

Screening for SARS-CoV-2 prior to Fetal Therapy

Why Screen?

Routine presurgical screening for SARS-CoV-2 is only relevant if a positive result can trigger interventions that may improve maternal or fetal outcome or positively impact family members, other patients, or HCW. A positive result might lead to patient isolation, delay or cancellation of surgery, and/or use personal protective equipment (PPE) by HCW. Asymptomatic patients who underwent major elective surgery under GA, who, in retrospect, were incubating COVID-19, all developed pneumonia; 44% were admitted to an ICU and 20% died from acute respiratory distress syndrome [40]. Their mean age (55 years, range 21–84) was not representative of pregnant women, but surgery under GA during viral incubation poses a higher risk of disease progression and complications than in comparable controls [43]. For patients undergoing less invasive surgery (including cesarean section), the risk was lower (8%) but still much higher than normal [40].

Elective surgery in SARS-CoV-2-positive patients should be avoided. Identification and isolation of SARS-CoV-2-positive patients also prevents the introduction of “super-spreaders” into hospitals, potentially infecting many patients and HCW [44], especially if undergoing aerosol generating procedures. Finally, there is the theoretical risk of vertical transmission during surgery in actively shedding patients.

How to Screen?

Screening strategies should be defined by local resource availability, result turnaround, and infection prevalence.

- Symptom questionnaires: screening for the most common COVID symptoms (cough, fever, dyspnea, nasal obstruction, anosmia [45]) can be easily implemented. Results are immediate, but false positives occur. This also does not identify asymptomatic carriers (reported in 6–14% of cases, depending on screening intensity) [46] [Deprest, pers. commun.] and patients may underplay symptoms for fear of being denied care.
- Nasopharyngeal (NP) swabs: NP swabbing for RT-PCR for SARS-Cov-2 RNA is currently the gold standard, being specific, but with a relatively high false

negative rate (due to inadequate sampling and rapid decline in viral load just prior to sampling) [47]. Negative results are also less relevant if delayed or if testing facilities or swabs are limited [48].

- Blood screening: infection with SARS-CoV-2 generates a typical antibody response, i.e., IgM and Ig G development after 12 and 14 days, respectively [34, 47, 49, 50], so antibody testing may be less useful acutely but could confirm a past infection. However, whether the presence of antibody actually confers immunity in COVID-19 is yet to be determined.

Who to Screen?

Based on current data, it seems logical to screen all patients entering a hospital (including women undergoing fetal interventions) using, at least, symptom questionnaires. NP swabs may be useful given that positive results would affect intra- and postoperative care. Screening by questionnaire and NP swabs should be done in women scheduled for major elective procedures, to minimize the risk of operating during the incubation period. A pending NP swab result should never delay any urgent surgery, but clinical questionnaire screening and PPE use in such cases is recommended.

We should consider whether to allow partner and visitor access to hospital if resources allow. Units may also want to screen asymptomatic HCW to prevent transmission of SARS-CoV-2 to patients or colleagues but also to prevent unnecessary HCW absences for symptoms attributable to allergies and other respiratory infections [48]. Questionnaire screening, followed by NP swabs in symptomatic HCW, is a possible strategy. Ultimately, antibody-specific serum screening could identify HCW who are COVID-19 immune, thus enabling their recruitment to teams caring for SARS-CoV-2-positive patients.

Postnatal Work-Up and Care of Neonates with Congenital Anomalies/Conditions during COVID-19

Resuscitation of a neonate born to a mother suspected or proven SARS-CoV-2-infection poses a risk to the neonate and HCW. The risks and benefits of delayed cord clamping, immediate separation of the infant versus skin-to-skin contact, and breast feeding should be reviewed with parents. Strict infection control measures during delivery, quarantine of infected mothers, and close monitoring of susceptible neonates are of paramount importance to reduce the risk of neonatal or HCW transmission.

If a mother is SARS-CoV-2 positive, neonates should be tested 24 h after birth. RT-PCR is the gold standard and a positive RT-PCR on NP/oropharyngeal or rectal swab is confirmatory [51]. RT-PCR accuracy can be affected by primer and probe differences. Depending on the sensitivity and specificity, result confirmation 24 h later is recommended.

ICU Care of a Neonate with SARS-CoV-2 Exposure

To date, there are no reports of neonates with congenital anomalies and concurrent COVID-19 infection. If one exhibited respiratory symptoms, chest X-ray might demonstrate the diffuse ground glass appearance, typical in adults, but neonatal radiographic criteria have not yet been established.

NICU infants should ideally be cared for within an isolate in a negative pressure room. Contact and droplet precautions are recommended, unless the infant is undergoing aerosol-generating procedures, e.g. deep suctioning, noninvasive ventilation such as continuous positive airway pressure, intubation/extubation, or mechanical ventilation, which mandate airborne precautions and full PPE. Given the common use of uncuffed tubes in neonates, both conventional and high-frequency ventilators are associated with some risk of aerosol generation.

Currently, evidence for maternal-neonatal transmission is limited. However, an asymptomatic mother could infect an infant during nursing and breast feeding. A routine face mask worn by the mother, next to hygienic measures, may help reduce such a risk.

Treatment of neonates with congenital anomalies or conditions should proceed as resources permit. Whenever possible, surgery should be delayed until COVID-19 testing is negative. Conversely, if surgery must be undertaken in a SARS-CoV-2-positive neonate or in a person under investigation, PPE must be used by the anesthetic, surgical, neonatal and nursing teams throughout. SARS-CoV-2 may be transmitted through multiple routes [52, 53]. Laparoscopic procedures lead to aerosolization and precautions include the use of a completely closed system, including insufflator, tubing, peritoneal cavity, and suction tubing with appropriate filters (viral dimensions are 0.06–0.14 μm) [54]. Desufflation should also occur in this closed system [52, 53].

The short-term outcome in SARS-CoV-2-positive neonates appears favourable, with most exhibiting only mild symptoms. So far, no neonates have been reported to develop severe COVID-19 pneumonia or die as a result of this illness [13, 31, 33, 55–57]. One reported seriously ill neonate

was probably symptomatic from prematurity and bacterial rather than viral infection [33]. Although no long-term developmental data on COVID-19-positive neonates exist yet, it is reassuring that the virus is not as neurotropic as other viruses. Pediatric COVID-19 infections seem to have a milder course and a better prognosis than adult cases, and deaths have been extremely rare. Fever and respiratory symptoms predominate, with few developing severe pneumonia [51]. There is no evidence that immunoglobulins, antivirals, or steroids improve outcomes.

Horizontal Transmission: Risks to HCW

SARS-CoV-2 poses a potentially serious risk to HCW [10]. This has led to a demand for testing of all pregnant women undergoing procedures, so that appropriate precautions can be taken if the screen is positive. With effective screening and testing in place, and appropriate PPE use, the risk of HCW transmission is probably low [51, 58]. This may not hold true when complex fetal operations are performed – necessitating many teams working in physical proximity, thus increasing the risk of exposure of multiple HCW. Any fetal surgery requiring (aerosol-generating) maternal intubation carries higher risks than procedures done under local or regional anesthesia [51]. Nevertheless, regional anesthesia or conscious sedation may require conversion to general anesthesia with intubation. Maternal NP testing should therefore be considered in any cases potentially requiring intubation.

The anesthesia team must wear appropriate PPE for airborne, droplet, and contact infection prior to intubation and extubation. In addition, insertion of a high-efficiency particulate air filter on the endotracheal tube and the use of in-line suctioning are important to reduce aerosolization [59–61]. If the surgical procedure is also aerosol generating, then all personnel in the operating room must wear PPE. If endotracheal intubation for general anesthesia is the only aerosol-generating portion of the procedure, the surgical and nursing personnel can stay outside of the operating room during intubation. After waiting 20–30 min (depending on the rate of air exchange in the room) to allow for evacuation of 99% of the aerosol from the atmosphere [62], the surgical and nursing personnel can then enter the room wearing standard PPE. The relative benefits of personnel protection need to be contrasted with the risk of added anesthesia time. Post-operative recovery of SARS-CoV-2 patients in the operating room and direct transfer to an isolation room afterward also helps to limit the exposure to additional HCW.

Resource Perspective

This pandemic is stretching healthcare systems, ICU, and PPE availability and it is stressing HCW. Many elective procedures have been cancelled and admissions for non-life-threatening conditions have diminished. Given this strain on resources, it is essential for each fetal treatment center to evaluate its own program and determine which procedures can or cannot be offered during this crisis, based on their local situation and available alternatives. It is perhaps logical to suspend fetal procedures of a greater complexity, given their use of HCW, potential need for ICU beds, and/or prolonged hospital admission [41]. In contrast, life-saving fetal blood transfusions and fetoscopic laser therapy for twin-twin transfusion syndrome can often be performed in outpatients or entailing a brief hospital admission. For SARS-CoV-2-positive patients requiring urgent fetal therapy, when and where to perform these procedures must be carefully considered. The loss of key personnel due to illness or redeployment may also adversely impact the ability to offer some fetal interventions. COVID-19 screening and/or testing and PPE use must be regularly reviewed and modified as fetal therapy demands and available resources change. In areas with multiple, perhaps even competing, fetal programs, this may be the time to work together and consolidate operations. In countries where national health systems commission fetal procedures, mitigation plans for these highly specialized services may be required.

Ethical Framework

Ethics in obstetrics provides us with a framework to guide management of pregnant women with SARS-CoV-2 infection. The principle of beneficence creates the obligation to provide management that deliberative (i.e., evidence-based, rigorous, transparent, and accountable) clinical judgment should result in a net clinical benefit. The ethical principle of respect for autonomy obliges caregivers to empower women to make informed decisions about their pregnancy care. This involves an informed consent process that provides information about reasonable care options including their benefits and risks, supporting her understanding and evaluation based on her own values and belief [63].

In the informed consent process for invasive prenatal diagnosis and interventions for fetal benefit there is no autonomy-based ethical obligation to provide a SARS-CoV-2-positive patient with information about theoretic

cal risks. The informed consent process for clinical investigation or maternal-fetal intervention should provide information about risks, based on prior investigation with animal and human subjects. A major purpose of clinical investigation is to identify and document such risks. Normally, identification of theoretical outcomes is excluded as a study objective and should not be included in the informed consent process. Moreover, discussion of theoretical benefits and risks can confuse or distract patients and does not empower informed decision making.

- Invasive prenatal diagnosis: there is currently no documented additional risk of pregnancy loss or fetal or maternal morbidity from invasive prenatal diagnosis in SARS-CoV-2-positive pregnant women [13]. In informed consent, there is no autonomy-based ethical obligation to provide information about undocumented additional risks of invasive procedures. It might reassure women who express concern to learn that there are no documented additional risks.
- Maternal-fetal intervention for fetal benefit: there is no documented additional risk of pregnancy loss, fetal harm, maternal morbidity or mortality, or neonatal harm from fetal interventions in SARS-CoV-2 positive pregnant women [1, 2]. No studies have explored fetal or neonatal risks. In informed consent, there is no autonomy-based ethical obligation to provide information about undocumented additional risks of fetal intervention. It might reassure women who express concern to learn that there are no documented additional risks.
- Use of resources: in a public health emergency, there is a beneficence-based ethical obligation of hospitals and HCW to reduce mortality risks in the affected population. To fulfil this obligation, hospitals may justifiably divert their material and human resources away from nonessential services. There is, however, a beneficence-based constraint: essential services such as obstetrics must continue to have sufficient resources, especially to prevent maternal and perinatal mortality. It is consistent with this constraint to suspend accepted maternal-fetal interventions that may not impact on perinatal mortality. Clinical trials do not do so; it is therefore consistent to suspend maternal-fetal trials.
- Restrictions on termination of pregnancy (TOP): where legally permitted, TOP is ethically justified when, following informed consent, a woman chooses TOP [4]. TOP is time sensitive and should never be classified as “elective,” even during a public health emergency [9, 3]. It follows that TOP restrictions, on

Table 2. Summary of recommendations

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- Routine antenatal care should be adjusted by spacing out appointments and using telemedicine and home-based care. US and noninvasive prenatal screening may also need rearrangement.
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- If resources allow, there may be a place for generalized testing of pregnant women for SARS-CoV-2 infection. We do recommend testing prior to any operative procedure.
-
- Pregnant women with SARS-CoV-2 infection may have a variable disease severity. It is uncertain whether they are at increased risk for COVID-19 disease. They should be managed based on the severity and nature of their complications. Cesarean delivery should be performed based on standard obstetric indications and considered in cases of septic shock or acute organ failure. Delivery *may* also facilitate maternal ventilation.
-
- There is minimal and unconfirmed evidence for *spontaneous* vertical transmission. This risk theoretically may be increased by fetal procedures by disruption of either the feto-maternal barrier or the fetal skin. One should avoid trans-placental instrument passage.
-
- Fetal therapy is time sensitive and hence should not be considered as elective care. In SARS-CoV-2 positive patients, one may consider delaying an intervention to avoid surgical morbidity, provided the procedure can wait. This applies, in particular, to complex procedures under general anesthesia and in symptomatic patients. Conversely, life-saving minimally invasive procedures should continue.
-
- Procedures of unproven fetal benefit should not be offered.
-
- When caring for a neonate born to a mother with suspected or confirmed COVID-19, strict infection control measures should apply, including quarantine. Based on current data, the spectrum of COVID-19 infection in neonates is usually mild, and their short-term outcomes are favourable.
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- HCW incur a significant risk of SARS-CoV-2 infection, which is an argument for testing patients. When caring for suspected or SARS-CoV-2-positive patients, appropriate personal protective equipment should always be used.
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- The COVID-19 pandemic does not strike equally around the world. Centers must periodically review and adjust their approach to fetal therapy as demands and available resources change.
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- When consenting women with SARS-CoV-2 infection for fetal procedures of proven benefit, there is no autonomy-based ethical obligation to provide information about *theoretical* risks. Informed consent provides information about reasonable options and their benefits and risks, and supports patient understanding and evaluation based on their own values and beliefs.
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- TOP is time sensitive and should not be considered as “elective.”
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- Registration of maternal and fetal outcomes is recommended because large cohort data will rapidly boost our knowledge.
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the grounds of being allegedly “elective” by governments [10], organizations, or payers, are ethically unjustified.

- Responsible management of the risk of horizontal transmission: The professional virtue of self-sacrifice creates the ethical obligation to take only reasonable risks to one’s self and other HCW [1]. Current evidence supports the deliberative clinical judgment that adherence to effective infection control measures reduces the incidence of horizontal transmission to levels similar to other infectious agents. To responsibly manage current uncertainty, it is compatible with the professional virtue of self-sacrifice to exempt pregnant HCW, because their future child cannot consent to exposure. It is also compatible with self-sacrifice to exempt HCW whose health or involvement in care provision may increase the risk of horizontal transmission.

Research in the COVID-19 Era

Registers of maternal and fetal outcomes should be supported to better understand this disease and to quantify pregnancy complications risks, such as miscarriage, growth restriction, stillbirth, preterm delivery, and vertical transmission. Larger cohort data will accelerate and improve our understanding, define appropriate measures for screening, confinement, and management, and guide disease prevention. This has been successful for other viral infections and it has rapidly boosted knowledge [64]. There is room for a coordinated approach to avoid interference or double registration [65–67], and data sharing should be encouraged [68]. We strongly endorse registries to evaluate whether fetal interventions affect maternal or fetal outcomes.

Conclusion

COVID-19 has put enormous stress on patients, HCW and healthcare systems. Nevertheless, fetal diagnosis and pregnancy care must be maintained, and we must strive to protect the vulnerable population of pregnant women and their fetuses. Our recommendations are summarized in Table 2. This includes both SARS-CoV-2-negative and SARS-CoV-2-positive women with fetal anomalies or conditions who may benefit from prenatal intervention. Multidisciplinary case discussion should include available resources. HCW should discuss with parents the risks and benefits of any procedure, including the possi-

bility of surgically induced morbidity. Ultimately, management decisions will depend on fetal and maternal condition and prevailing local circumstances.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflict of interests to declare.

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