

RESEARCH LETTER

SARS-CoV2 (COVID-19) infection: is fetal surgery in times of national disasters reasonable?

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Abstract

Even though the global COVID-19 pandemic may affect how medical care is delivered in general, most countries try to maintain steady access for women to routine pregnancy care, including fetal anomaly screening. This means that, also during this pandemic, fetal anomalies will be detected, and that discussions regarding invasive genetic testing and possibly fetal therapy will need to take place. For patients, concerns about Severe Acute Respiratory Syndrome-Corona Virus 2 will add to the anxiety caused by the diagnosis of a serious fetal anomaly. Yet, also for fetal medicine teams the situation gets more complex as they must weigh up the risks and benefits to the fetus as well as the mother, while managing a changing evidence base and logistic challenges in their healthcare system.

1 | INTRODUCTION

In this letter, we as fetal therapy specialists, want to address some of the particularities that will need to be taken into account when considering fetal interventions during the SARS-CoV2 pandemic. Our aim is to open a discussion within the fetal medicine community and to enable centres who are ahead of us 'on the curve' to comment and share their experiences. This will complement other guidelines on pregnancy care, labour and delivery in the COVID-19-era.¹⁻⁴

2 | VERTICAL TRANSMISSION DURING FETAL PROCEDURES

Strong data on vertical transmission of SARS-CoV2 from mother to fetus are lacking.⁵ So far, no proven cases of spontaneous vertical

transmission have been published, but only limited numbers of mother-child pairs have been examined.⁶⁻⁸ Moreover, in most cases, mothers were infected in the third trimester of pregnancy and fetuses delivered very rapidly after the onset of symptoms, thereby limiting the time for potential in utero transmission. Neonatal symptomatic cases have been described⁹ and one report describes the presence of SARS-CoV2 IgM antibodies in the serum of a neonate at 2 hours of age, suggesting that the fetus may have been exposed to the virus in utero.¹⁰

From a fetal intervention perspective, we need to appreciate that doing an invasive procedure in a SARS-CoV2 positive woman potentially increases the risk of vertical transmission, similar to what was observed in HIV positive women prior to the introduction of antiviral therapies. Based on current evidence, outcomes of COVID-19 in healthy neonates are usually good.^{6,7,9,11,12} Viral transmission earlier in gestation, as well as infection of an already sick fetus could nevertheless lead to worse outcomes.

At present, concerns for vertical transmission should not prevent clinically indicated minimally invasive procedures such as amniocentesis or fetoscopy from happening. However, we would recommend avoiding transplacental access, as the latter increases the risk of intra-amniotic bleeding and disruption of the feto-maternal barrier. Additionally, if possible, we would recommend delaying the intervention until the mother has cleared the infection by for example choosing to replace a chorionic villus sample with an amniocentesis (Table 1). With open fetal surgery, the risk of mother-child transmission is likely higher than with needle and fetoscopic procedures as the fetus is exposed to more maternal blood and the fetal skin integrity is usually breached in these interventions. We would therefore recommend postponing these interventions until after maternal clearance of the virus.

3 | MATERNAL CONSIDERATIONS

SARS-CoV2 *negative patients* planned to undergo fetal intervention should be informed that exposure to healthcare professionals, other patients or hospital staff increases their risk of contracting the virus. Similarly, patients travelling to access the service may expose themselves to higher infection risks. For international travel, additional restrictions may have to be tackled, or patients may find themselves temporarily 'trapped' far away from home after the surgery. Strict application of hand hygiene and social distancing as well as the appropriate use of protective equipment is recommended. Patients should also be aware that, if they develop COVID-19, the pregnancy and fetal outcomes may be worse than what has been described in studies with non-infected patients. Indeed, COVID-19 in pregnancy likely increases the risk of preterm birth and possibly also fetal growth restriction.⁵

The risk for an *asymptomatic SARS-CoV2-positive pregnant mother* to progress to overt COVID-19 disease is unknown, though most sources quote it as 'low' and not higher than health- and age-equivalent women.^{1,13} Nevertheless, the physiological changes of pregnancy may predispose pregnant women to higher risk for cardiorespiratory instability.⁵ To avoid the coincidence of iatrogenic maternal surgical morbidity with additional infection-related problems, it may seem prudent – if the fetal condition allows – to delay fetal interventions until the mother has cleared the viral infection, which at present is said to be after 14 days in an asymptomatic woman.¹⁴ Additionally or alternatively, one could wait until after two consecutive negative screening tests, though that is debatable given it can be false negative by then and uses additional resources. For complex surgeries under general anaesthesia, one may need to be more restrictive. A retrospective study of COVID-19 patients, who were asymptomatic when they had an elective operation under general anaesthesia, reported a 40% risk of admission to ICU and a 20% mortality rate.¹⁵ Even though the population demographics (average age: 55; range 21-84) did not overlap with that of young pregnant women, it seems that patients unintentionally scheduled for surgery during the incubation period are at higher risk for disease progression than controls.¹⁶

What's already known about this topic?

- Pregnant women who get infected with SARS-CoV2 do not seem to have a worse disease course than non-pregnant women.
- SARS-CoV2 infection in pregnancy can cause preterm birth and fetal growth restriction.
- SARS-CoV2 infected patients can contaminate care givers.

What does this study add?

- Risk for spontaneous vertical transmission seems low, but it seems prudent to avoid transplacental surgical access during invasive procedures.
- We suggest to balance the fetal benefit of evidence-based therapies against the potential risks for the fetus, mother and healthcare providers.
- Each unit should review local resources and emerging evidence to assess their ability to provide a fetal therapy program.

For *symptomatic SARS-CoV2-positive women*, it is equally preferable to delay fetal interventions whenever possible. First, because the typical symptoms of COVID (coughing and dyspnoea) may interfere with safe surgery. Second, because additional surgical stress may trigger worsening or faster progress of the disease and iatrogenic complications.¹⁷ A clear example of such scenario is prenatal spina bifida closure, which is always done under general anaesthesia and inherently has an increased risk of post-operative severe respiratory problems.¹⁸ Delaying fetal surgery seems more prudent, or even postponing repair until after birth, if it cannot be done in the optimal gestational age window, because fetal benefits decrease with gestation, with unproven benefits beyond 26 weeks of gestation.¹⁹

For *any SARS-CoV2-positive women*, it is obvious that investigational procedures or interventions with unproven benefit (Table 1), should not be performed. Conversely, for selected conditions of proven benefit, intervention may still be considered. One such example is fetoscopic laser ablation of placental anastomoses for twin-twin transfusion syndrome. Indeed, in most cases postponing these interventions leads to fetal death or severe preterm birth. Additionally, amniodrainage, which is part of the surgery, will improve the maternal respiratory status. Finally, this intervention can be done under local anaesthesia and the added maternal morbidity of fetoscopic procedures is low.¹⁷ Along the same lines, we would consider offering fetal transfusions and thoraco-amniotic shunting for fetal hydrops due to pleural effusions (Table 1).

TABLE 1 Diagnostic and therapeutic procedures, estimated risks and benefits and position based on current knowledge and available resources. Rare conditions and procedures will need to be discussed on a case-by-case basis.

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 patient. Delay to amniocentesis in symptomatic and screen positive patient
Amniocentesis	High	Low	Low	Unlikely	Minimal	Offer to asymptomatic patient; others consider delay if possible
Fetal blood transfusion	High	Moderate	low	Unlikely	Moderate	Offer to screen negative patient, adjust for symptomatic or screen positive patient if 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 patient, adjust for symptomatic or screen positive patient if cannot be delayed
Vesico-amniotic shunting	Low	Moderate/High	Low	Unlikely	Moderate	Consider not offering
Fetal cystoscopy	Unknown	Moderate/High	Low	Unlikely	Moderate	Consider not offering
Laser for TTTS	High	Low	Low	unlikely	Moderate	Offer to asymptomatic patient, adjust for symptomatic or screen positive patient, if cannot be delayed
Selective feticide in monochorionic twins	Variable	Low	Low	Unlikely	Moderate	Offer to asymptomatic patient, adjust for others
Tracheal occlusion for CDH	Unknown	Low	Low	Unlikely	Moderate	Consider not offering
Spina bifida closure	High	High	Moderate/High	Low	High	Delay if gestational age allows. If not, offer only to screen negative patient if sufficient local resources are available.

Abbreviations: CDH, congenital diaphragmatic hernia; TTTS, twin-to-twin transfusion syndrome.

4 | RISKS TO HEALTH CARE WORKERS

Similar to what is seen with other maternal viral infections, there is the additional dimension that COVID-19 poses a serious health risk to health care workers.¹ This is the drive for screening women undergoing procedures, so that maximal precautions can be taken when patients are positive. With screening policies in place, as well as judicious use of personal protective equipment, the risk of infecting staff in the workplace is likely low.²⁰ Complex fetal surgeries however, rely on close cooperation of multiple teams in a small space, thereby carrying the risk of contamination of a large number of staff and spreading of the virus throughout the hospital. Lastly, fetal surgeries requiring maternal intubation (which is an aerosol generating procedure) expose hospital staff to much higher risks than procedures under local or loco-regional anaesthesia.²¹

5 | RESOURCE PERSPECTIVE

At present, healthcare systems are tremendously stretched for ICU beds, medical personnel and personal protective equipment. This has led to delaying interventions and admissions for non-life-threatening conditions. Along this line, it would seem logical in certain places to also suspend offering fetal procedures of large complexity given their potential requirements for maternal ICU beds and/or long-term maternal hospital admission.¹⁷ For COVID-19 patients, there is the additional complexity of management of pregnant patients in remote and isolated cohort wards by two teams. Units should also reflect on whether they can ethically maintain highly demanding fetal therapy programs when staffing becomes scarce due to illness or redeployment to 'high-volume' departments such as the medical wards or ICU wards. In geographic areas with multiple (competing) fetal therapy programs, this may also

be the time to work together, downscale and refer. In countries where national health systems commission fetal procedures, a mitigation plan for these highly specialised services may need to be designed.

6 | CONCLUSION

The COVID-19 crisis puts a previously unwitnessed stress on patients, care givers and healthcare systems. Nevertheless, 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. Cases should be discussed ad hoc by a multi-disciplinary team that also takes into account the available local and national resources. The team should have an individualised discussion with the prospective parents about the risks and benefits of the procedure involved, including the likelihood of postoperative respiratory problems. The ultimate balance will be dependent on the fetal condition and local circumstances at that moment.

We are looking forward to hear and learn from other fetal therapy programs on how they managed patients and resources in these difficult times.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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