

Coronavirus disease (COVID-19) The obstetrical view

In December 2019, a number of patients with pneumonia of unknown cause, presented in Wuhan, China¹. As of March 11th 2020 the infection has been declared as a pandemic by the WHO². A previously unknown betacoronavirus was isolated from human airway epithelial cells, and was named 2019-nCoV, the seventh member of coronavirus family that affects humans³.

Coronavirus are enveloped RNA viruses, that are common in humans, mammals and birds. Of the 6 previously known coronavirus affecting human, 4 (229E, OC43, NL63, and HKU1) are prevalent and typically cause common cold symptoms in immunocompetent individuals.

The two other strains — severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have been linked to fatal illness.

SARS-CoV was the cause of the severe acute respiratory syndrome outbreaks in 2002 and 2003 originating in China^{4,5}. MERS-CoV was the pathogen responsible for the middle eastern outbreak of severe respiratory disease in 2012⁶. Given the high prevalence and wide distribution of coronaviruses, the large genetic diversity and frequent recombination of their genomes, and increasing human–animal interface activities, novel coronaviruses are likely to emerge periodically in humans owing to frequent cross-species infections and occasional spillover events.

To the current date⁷, 2019-nCoV has infected 144,863 globally, most cases in China, Iran, Italy, South Korea, France, Spain, Germany and the United States. Canada has currently 191 confirmed patients, 74 of which are in Ontario. Reported numbers are likely underestimates of the true numbers since milder cases are less likely to be reported.

Clinical Manifestations

2019-nCoV spreads from human to human by means of airborne droplets, coughing and sneezing, close personal contact, it is currently not known if the virus can spread by sexual intercourse.

2019-nCoV causes an illness ranging in severity from the common cold to severe respiratory illness and death.

Up to now the average age of hospitalized patients has been 49-56 years, with a third to half with an underlying illness, more frequently male. Children have been rarely reported. As previously reported by NYGH staff, the first confirmed paediatric case in Ontario was a 3-month old baby boy who came into NYGH's ED this week and was diagnosed with COVID-19. He was in close contact with his grandfather who was diagnosed at NYGH last week. The baby had mild symptoms and did not require admission.

Frequent manifestations include fever, productive cough, myalgia, headache and diarrhea. Abnormal testing includes abnormalities on chest radiographic imaging, lymphopenia, leukopenia and thrombocytopenia.

Initial reports suggest that acute respiratory distress syndrome (ARDS) develops in 17-29% of hospitalized patients. Overall case fatality rate appears to be ~1%, while fatality rates have ranged from as low as 0.7% to as high as 4.9%.

Risk factors for severe illness and mortality, include elderly age, male, presence of comorbidities (HTN, DM, coronary heart disease), higher respiratory rate, higher SOFA/qSOFA scores, leukocytosis, Elevated creatinine and liver enzymes and elevated troponin levels⁸

2019-nCoV infection during pregnancy

Currently, there is limited information from published reports about 2019-nCoV in the obstetric population^{9,10}. Available data are reassuring but are limited to small case series. In general, pregnant women experience immunologic and physiologic changes that make them more susceptible to viral respiratory infections, potentially including 2019-nCoV.

It is reasonable to predict that pregnant women might be at greater risk for severe illness, morbidity, or mortality compared with the general population, as is observed with other related coronavirus infections including SARS-CoV and MERS-CoV, and other viral respiratory infections, such as influenza, during pregnancy. Data from MERS-CoV and SARS-CoV, although limited, suggest that infection in pregnancy may be associated with severe infection and adverse neonatal outcomes, including increased risk of miscarriage, fetal growth restriction, and preterm birth.

2019-nCoV in pregnancy

Susceptibility to 2019-nCoV Infection Although data are limited, evidence from SARS and MERS, do not imply that pregnant women are more susceptible to infection with coronavirus.

There are no direct data to inform whether pregnancy increases susceptibility to 2019-nCoV.

Clinical manifestation and disease severity in the pregnant patient - In a study by Chen et al⁹, nine women diagnosed with 2019-nCoV during the third trimester of pregnancy were reported. In this small series, clinical presentation was similar to that seen in nonpregnant adults, with fever in seven, cough in four, myalgia in three, and sore throat and malaise each in two women. Five had lymphopenia. All had pneumonia, but none required mechanical ventilation, and none died. All women had a cesarean delivery, and Apgars were 8-9 at 1 minute and 9-10 at 5 minutes.

In a second series of nine pregnancies with ten infants (one set of twins) reported by Zhu et al¹⁰, symptom onset was before delivery in four, on the day of delivery in two, and after delivery (1-3 days) in three cases. Clinical presentation of 2019-nCoV was similar to that seen in nonpregnant patients. Among the nine pregnancies, intrauterine fetal distress was noted in six, seven were cesarean deliveries, and six infants were born preterm. Based on these limited reports, and the available data from other respiratory pathogens such as SARS and influenza, it is unknown whether pregnant women with 2019-nCoV will experience more severe disease.

Vertical transmission Limited experience with newborn evaluations after delivery with SARS and MERS has not identified cases of maternal-to-fetal transmission. Data from the recent case series published by Chen⁹ and Zhu¹⁰ et al of 19 infants to mothers infected in the third trimester of pregnancy with SARS-CoV-2 identified no laboratory evidence of vertical transmission. Testing of amniotic fluid, cord blood, and neonatal throat swab samples was negative for SARS-CoV-2 in the six patients reported by Chen et al. In

the report by Zhu et al some infants were symptomatic; however, throat swab testing of all infants was negative for SARS-CoV-2.

At this time, it is unknown if SARS-CoV-2 can be transmitted from mother-to-fetus.

Management of patients and suspected patients

Currently, no coronavirus-specific treatments have been approved for use.

Reducing infection risk - Measures for reducing the risk for infection and infecting others with 2019-nCoV include frequent hand washing, coughing or sneezing in a flexed elbow or tissue, avoid touching your eyes, nose and mouth with unwashed hands, avoid close contact with symptomatic individuals, cleaning and disinfecting frequently touched objects and wearing a mask if symptomatic or caring for a patient with symptoms.

Diagnosis Individuals who exhibit symptoms of 2019-nCoV and have had close contact with a laboratory-confirmed 2019-nCoV patient, within 14 days of symptom onset, or have a history of travel from affected geographic areas within 14 days of symptom onset, be tested while other causes of illness are excluded. Current testing is by polymerase chain reaction (PCR). Computerized tomography (CT) imaging may be useful as an adjunct to diagnosis, as there are potentially pathognomonic findings for 2019-nCoV including ground-glass opacities.

Management of the pregnant patient

Reducing infection risk - Pregnant women who have severe chronic medical illnesses such as heart, lung, should follow the CDC precautions for those at higher risk of severe illness, including general practices as stocking up on supplies, keeping away from others who are sick, limiting close contact, and frequent hand washing. Further, the CDC recommends avoiding crowds, unessential travel and staying at home as much as possible¹¹.

Diagnosis of the pregnant patient – preferred method of diagnosis is PCR, and pregnancy does not seem to alter test performance. If CT imaging is considered to evaluate a pregnant patient with suspected or confirmed 2019-nCoV infection, the usual guidance regarding the risks and benefits of diagnostic radiation in pregnancy is warranted.

Treatment - Because 2019-nCoV might increase the risk for pregnancy complications, management should be in a health care facility with close maternal and fetal monitoring. Principles of management of 2019-nCoV in pregnancy include early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, empiric antibiotics (secondary to bacterial infection risk), co-infection testing, fetal and uterine contraction monitoring, early mechanical ventilation for progressive respiratory failure, individualized delivery planning, and a team-based approach with multi-specialty consultations. Team-based management is recommended for pregnancies managed in a health care facility and should include a determination of the optimal clinical unit on which to provide care. Ability to provide surveillance for early detection of a worsening maternal course of illness, as well as an ability to monitor for evidence of obstetric complications (e.g., preterm labor or fetal compromise), are needed. Changes in fetal heart rate pattern may be an early indicator of maternal respiratory deterioration. Based on experience with SARS and MERS, severe respiratory failure might occur in pregnant women, and in the most severe cases, mechanical ventilation might not be sufficient to support adequate oxygenation. If that occurs, limited literature suggests a potential role of extracorporeal membrane oxygenation (ECMO) in pregnancy; use should only be considered in centers that have

experience with this technique. Whether delivery provides benefit to a critically ill mother is unknown; decisions regarding delivery should consider the gestational age of the fetus and should be made in conjunction with the neonatologist.

Antepartum care – The SOGC has published a committee opinion regarding 2019-nCoV in pregnancy¹². Obstetrical patients with respiratory symptoms should be asked to wear a surgical mask immediately upon presentation to the health care facility.

Women suspected of having or having been exposed to COVID-19 should be triaged quickly, given a mask to wear, and transferred to a single-occupancy room as quickly as possible.

Testing should be performed as per local guidelines and recommendations. Pregnancy does not appear to alter test performance.

Expectant management at home may be appropriate for many women. For women requiring admission, droplet/contact infection precautions are adequate.

Health care providers should consider delaying routine antepartum care appointments for women who have or are being tested for COVID-19. Self-quarantine as per local protocols is appropriate.

The use of N95 respirators is only required for aerosol-generating procedures (e.g., intubation). The duration and discontinuation of precautions should be determined in accordance with Public Health Agency of Canada guidelines, and provincial and territorial guidance.

Health care providers can consider empiric antibiotic therapy for superimposed bacterial pneumonia in women with confirmed COVID-19 infection or severe respiratory disease. First-line antibiotics are oral amoxicillin for stable patients and ceftriaxone for severe disease, based on general recommendations for the management of pneumonia.

For maternal surveillance, close monitoring or initiation of an obstetrical early warning system is appropriate.

Initiation of antepartum corticosteroids for fetal maturation could be considered as per current guidelines if preterm delivery is indicated or anticipated based on maternal condition.

Antepartum fetal surveillance of confirmed cases of COVID-19 should occur monthly and include fetal ultrasound assessment for growth and anatomy.

Intrapartum care

Droplet/contact precautions should be used, including wearing a surgical mask with eye protection, a gown, and gloves.

Use of N95 respirators should be reserved for aerosol-generating procedures (e.g., intubation).

Unnecessary health care personnel in the room should be minimized.

It is advisable to limit the presence of symptomatic family and household contacts in the delivery suite and visitation should be permitted in accordance with locally developed infection prevention and control protocols.

Intrapartum fetal monitoring in the form of EFM should be considered given evidence showing fetal distress during labour.

Cesarean delivery should be reserved for obstetrical indications.

There is no data to indicate that the second stage of labour generates aerosols and, as such, droplet/contact precautions are sufficient for vaginal delivery.

Given that intubation is considered an aerosol-generating procedure, the surgical team should wear N95 respirators for cesarean delivery in case there is a need to convert from neuraxial to general anesthesia.

There is no evidence to avoid delayed cord clamping or to encourage early cleansing of the infant.

Routine practices such as skin-to-skin contact (with the mother wearing a mask and after having washed her hands) and delayed cord clamping should continue.

Elective cesarean delivery should be delayed, if possible, until a woman is no longer considered infectious.

Appropriate patient transfer planning should be made so as to minimize exposure of other patients in the hospital.

Hospital birth is preferred to home birth for women who have or are being tested for COVID-19, in light of the challenges associated with ensuring appropriate personal protective equipment in the home setting and the high rates of fetal distress that reported in the literature.

Mother and neonate after delivery The CDC recommends that facilities should consider temporarily separating a woman with suspected or confirmed 2019-nCoV from her infant until the woman's transmission-based precautions are discontinued. The SOGC does not endorse this recommendation. Women should practice good handwashing before and use of a mask while engaging in infant care.

Given the current lack of information regarding vertical transmission, it seems reasonable to assume that a newborn born to a mother with 2019-nCoV at delivery could possibly be infected, either in utero or perinatally, and should be placed in isolation from other neonates to avoid exposure.

Regardless of the gestational age at which a pregnant woman was infected COVID-19, the newborn infant should be tested for COVID-19 at birth (i.e., nasopharyngeal swab and umbilical swab for COVID-19 polymerase chain reaction)

Breastfeeding - Chen et al. found no evidence of 2019-nCoV in the breast milk of 9 infected women. Breastfeeding is encouraged and is a potentially important source of antibody protection for the infant. The CDC recommends that during temporary separation, women who intend to breastfeed should be encouraged to express their breast milk to establish and maintain milk supply. If possible, a dedicated breast pump should be provided. Before expressing breast milk, women should practice appropriate hand hygiene. After pumping, all parts of the pump that come into contact with breast milk should be thoroughly disinfected. Expressed breast milk should be fed to the newborn by a healthy caregiver. For women and infants who are not separated, the CDC recommends¹³ that if a woman and newborn do room-in and the woman wishes to feed at the breast, she should put on a facemask and practice hand hygiene before each feeding.

Pregnant Healthcare personnel and 2019-nCoV- Health care personnel (HCP) risk for exposure to 2019-nCoV is divided into 3 groups by the CDC, High risk (prolonged contact, not wearing a mask while exposed to aerosol producing procedures) medium risk (protective gear during aerosol producing procedure) and low risk (brief interaction with 2019-nCoV patient, wearing a mask and eye protector during exposure).

Although no formal guidelines and recommendations exist on the subject, it seems reasonable to limit the exposure of pregnant HCP to 2019-nCoV patients, for high risk and medium risk exposure, as the severity of disease may be more severe in this sub population and as the fetal/neonatal risks are not clear at this present time.

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