Osteopathic Considerations for the Pregnant Patient With COVID-19

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In any given year, approximately 130 million babies are born worldwide. Previous research has shown that pregnant women may be more severely affected and vulnerable to contracting emerging infections, making them a particularly high-risk population. Therefore, special considerations should be given to treatment methods for pregnant women with COVID-19. In this narrative review, the authors evaluate scholarly journal articles and electronic databases to determine what is known about the pathophysiology of COVID-19 in pregnancy and the associated mortality rate. Osteopathic manipulative treatment techniques to mitigate the underlying pathology were identified, and modifications for use in pregnancy and the critical care setting are described.

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As of 2016, there were approximately 130 million babies born each year worldwide, and about 4 million were born in the United States.¹ Previous research has shown that pregnant women may be more severely affected by and vulnerable to contracting emerging infections, making them a particularly high-risk population.^{2,3} As such, special considerations should be given to treatment methods for pregnant women during the current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, or COVID-19) pandemic. Recent evidence suggests that the unique physiological state of pregnant women presents both potentially protective and harmful effects with respect to COVID-19.

In this narrative review, we evaluated publications from electronic databases (PubMed, Cochrane Library, and Google Scholar) to outline the current literature regarding maternal health outcomes during coronavirus outbreaks. The majority of this data has been published within the last 1 to 2 years and was focused on the impact of novel coronavirus epidemics, including severe acute respiratory syndrome virus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and COVID-19, during pregnancy. The articles we reviewed also discussed the benefits of and modifications for OMT in pregnant patients. Here, we discuss the effects of COVID-19 on maternal health outcomes and OMT modifications that can be used for pregnant women with COVID-19 in inpatient and outpatient settings.

COVID-19 and Pregnancy

Coronaviruses, including enveloped RNA viruses like SARS-CoV, MERS-CoV, and COVID-19, result in illnesses ranging from the common cold to severe respiratory

illness and death.⁴ Common symptoms of COVID-19 in pregnant patients are fever, cough, fatigue, diarrhea, dyspnea, sore throat, and myalgias.⁵ On a molecular level, COVID-19 preferentially infects host respiratory epithelial cells by binding to ACE-2 located predominantly on Type II pneumocytes.^{6,7} ACE-2 expression is enhanced in pregnancy and is found in other tissues such as the digestive tract, placenta, and uterus.^{6,8,9}

Mortality rates of COVID-19 in pregnancy have been challenging to quantify because of limited publications of mostly smaller case series and observational cohorts. Novel coronaviruses have historically resulted in higher mortality rates for pregnant patients than nonpregnant patients.¹⁰ Maternal case-fatality rates have been documented as high as 25% and 27% for SARS-COV and MERS-COV, respectively.^{4,10} Though case series regarding pregnant women with COVID-19 are ongoing, emerging research evaluating COVID-19 in pregnancy suggests that it may be less lethal when compared with SARS-COV and MERS-COV.¹⁰ A recently published systematic review⁵ showed that clinical characteristics of pregnant women with COVID-19 may be similar to those of nonpregnant adults. However, symptoms of COVID-19 such as dyspnea, nasopharynx hyperemia, and nasal congestion may be falsely attributed to normal pregnancy changes, resulting in underutilization of testing or delays in care. Recently published research investigating characteristics of reproductive-age women with COVID-19 infection has demonstrated that pregnancy has been associated with increased rates of hospitalization, increased risk for intensive care unit admission, and increased receipt of mechanical ventilation, but not with increased mortality rates.¹¹

Fetal Consequences

Fetuses and newborn infants may be particularly vulnerable to acquiring COVID-19 and to the consequences of infection. Fetuses and neonates possess adaptive and innate immune systems that are not fully developed, creating a physiological environment

vulnerable to infection.¹² The capability of vertical COVID-19 transmission is therefore of great research interest. Emerging evidence on this topic suggests that COVID-19 may be transmitted from mother to fetus, and it has been suggested that COVID-19 be included in the grouping of toxoplasmosis, rubella cytomegalovirus, herpes simplex, and HIV (“TORCH”) newborn infections.¹³

Regarding fetal and neonatal mortality, a recent systematic review of 108 pregnancies with COVID-19 positive mothers indicated 1 fetal death and 1 neonatal death.¹⁴ More research is needed to determine the risks and effects of COVID-19 transmission to fetuses and newborns. There are no studies that suggest that OMT may increase or decrease the risk of placental viral transmissions. Studies have shown that OMT may be beneficial for neonates in the intensive care unit (ICU) and is effective in reducing the hospital length of stay, which may be helpful for COVID-19-positive neonates.¹⁵

Protective Physiologic Changes

The unique hormonal and immunological state that presents in pregnancy may be protective against COVID-19. Immunologically, pregnant women have been shown to be in a predominantly cell-mediated T-helper 2 (Th2) state (compared to the non-pregnant, predominantly humoral T-helper 1 state), referred to as Th1-Th2 shift.^{3,16} Each T-helper cell type secretes cytokines, which may be pathogenic or protective. Th1 cells secrete Interferon-gamma (IFN- γ) and tumor necrosis factor alpha (TNF), which are proinflammatory, while Th2 cells secrete interleukin (IL)-4 and IL-10, which are anti-inflammatory. Limited data suggest that pregnant individuals are not at increased risk for mortality from COVID-19, possibly due to pregnancy being predominantly a Th2 state, resulting in less severe lung damage.^{3,14} Nonpregnant individuals in a predominantly Th1 response state would be expected to respond to COVID-19 with increased proinflammatory cytokines, which may explain the increase the nonpregnant patient’s risk of mortality.⁶

Potentially Adverse Physiologic Changes

Pregnant patients in whom the Th2 state fails to make a more robust Th1- Th2 shift may be at higher risk for worse infection outcomes¹⁷; this may explain the poorer outcomes in some pregnant patients with COVID-19. Pregnancies with a Th1 proinflammatory profile are susceptible to spontaneous loss, growth restriction, and preterm labor. Studies have shown that prenatal prophylactic OMT may help decrease the risk of these complications.¹⁸ Other pregnancy related changes include a decrease in functional residual capacity and a 20% to 33% increase in oxygen consumption.¹⁹ With respiratory illness, these physiologic changes negatively impact a pregnant patient's ability to clear excretions, decreasing oxygenation saturation and risking hypoxia in both mother and fetus.

Management

Current treatment modalities for COVID-19 are supportive and include management of complications from sepsis and ARDS. Medical management is experimental at this time.⁴ Remdesivir is an antiviral that may prevent viral replication of COVID-19 in vitro and appears to be safe in pregnancy.²⁰ Protease inhibitors that interfere with viral replication have not been shown to be teratogenic. Ribavirin, an antiviral medication, is teratogenic and should be avoided in pregnancy due to the increased risk of craniofacial and limb defects in addition to spontaneous abortion.²¹ Chloroquine is an antimalarial drug that has demonstrated controversial efficacy and recommendations for its use have now been retracted.²² A lack of randomized controlled trials limits our full understanding of the efficacy and appropriate doses for the proposed medications used to treat COVID-19; this is particularly true in pregnancy. When compared with the lack of scientific consensus regarding the safety and efficacy of these drugs, OMT appears to offer a sensible management plan, as OMT has been proven to be safe, effective, and affordable.

Management considerations in pregnancy are subtle but important. Oxygen saturations must be maintained

above 95% to assume sufficient fetal oxygenation.⁴ Pregnancy is a state of respiratory alkalosis with a normal arterial pH of 7.40 to 7.47. Metabolic compensation for this reduces serum bicarbonate to approximately 20 mEq/L with a base excess of 2 to 3 mEq/L.¹⁹ Noninvasive ventilation such as continuous positive airway pressure or bilevel positive airway pressure is generally avoided in pregnancy because of increased aspiration risk from relaxation of the lower esophageal sphincter and should be avoided in patients with COVID-19 given the high risk of aerosolization. High-flow nasal cannulae, while considered an aerosolizing treatment, are increasing in use as ventilators become scarce. Given these limitations, early intubation is recommended when a pregnant patient has suspected respiratory distress, as physiologic laryngeal edema can make intubation attempts in pregnancy 8 times more likely to fail.²³ With the growing concern over ventilators availability as well as clinical observations suggesting difficulty in extubating the patient with COVID-19,²⁴ treatment modalities that avoid intubation or decrease the duration of ventilation must be sought.

Early self-proning or rotating has demonstrated improved oxygen saturation in nonpregnant patients with COVID-19.²⁵ Studies have shown that proning can be comfortable and feasible in pregnant women even at term for short periods.²⁶ After 34 weeks, prone positioning provides relief of uterine compression off of maternal vessels and decreases the systolic/diastolic ratio of the fetal umbilical artery, indicating decreased resistance to placental blood flow.²⁷ Based on our institution's experience and that of other published case studies,^{28,29} prone positioning without sedation or invasive ventilation has been a safe and efficient adjunct to support oxygenation in pregnancy affected by COVID-19 infection. While this positioning requires special support pillows for pregnant patients to ensure direct pressure is not applied to the uterus, pregnancy is not an absolute contraindication to prone positioning.

Osteopathic manipulative treatment (OMT) considers that structure and function are interrelated. The

normal physiologic changes of pregnancy predispose these patients to structural changes affecting both the respiratory and cardiovascular systems.¹⁹ When used as adjuvant therapy, OMT has been shown to decrease mortality in respiratory failure, decrease the incidence of pneumonia, and thus decrease the length of hospital stay.³⁰ The goals of using of OMT in the pregnant patients with COVID-19 include optimizing pulmonary respiration, facilitating drainage of the venous and lymphatic systems, and optimizing autonomic nervous system function. Stenta et al³¹ have outlined management strategies to enhance lymph drainage from the lung interstitium to reduce the demand for mechanical ventilation. We propose the following additional techniques, including rationale for use and pregnancy modifications in [Table 1](#).

OMT Modifications for Pregnant Patients With COVID -19

In general, OMT techniques have not been proven to increase aerosolization of respiratory particles; however, certain techniques may cause forceful expiration and therefore carry the potential for aerosolization. Examples include rib raising, lymphatic pump techniques (particularly thoracic or pedal pump), or any technique that may induce coughing, such as redoming of the diaphragm or deep inhalation techniques. As OMT requires hands-on care, it is necessary to wear appropriate personal protective equipment (PPE) as indicated by the CDC³² or institutional policy when caring for patients either suspected of or diagnosed with COVID-19. We advise the following respiratory PPE for potential aerosol-generating procedures including OMT:

- Patients with negative COVID-19 → Ear-loop mask + eye protection
- Patients with suspected or confirmed COVID-19 → N95 + face shield/eye protection

In addition, patients should be encouraged to wear an ear-loop mask when in the office and when unable to

avoid close proximity to others. The patient's face should be turned to the side when possible during treatment to limit exposure.

Contraindications for OMT in pregnancy or with suspected COVID-19 include inadequate PPE, patient instability requiring more rapid therapy, fetal instability requiring delivery, lower extremity deep vein thrombosis, coagulopathies, vaginal bleeding or threatened/incomplete abortion, preterm labor, or the inability to safely modify a given technique for pregnancy.

Inpatient technique modifications for all patients (both pregnant and non-pregnant) requiring advanced airway support include:

- Minimizing frequent and multiple position changes,
- Recruiting an assistant to ensure airway support is maintained during position changes,
- Performing techniques in the semi-seated (Fowler's) position at an angle of 30 degrees if already intubated, and
- Performing techniques in the left lateral recumbent position with an assistant present to ensure airway support is maintained.

While prone positioning has been viewed as less desirable for OMT (given that seated or lateral recumbent modification can be made), prone positioning for respiratory distress is not contraindicated and is in fact encouraged. If patients are in prone position for respiratory indications, it is reasonable to perform OMT in these positions regardless of gestational age.

Outpatient modifications for pregnant patients based on trimester of gestation include:

- <14 weeks gestation: The supine position is appropriate as the gravid uterus is not yet sufficiently large to cause aortocaval compression.
- 14-32 weeks gestation: Avoid prolonged treatment in the supine position. We recommend utilizing technique modifications identified in [Table 1](#).
- >32 weeks gestation: Recommend against treatment in the supine position for pregnancies of advanced

Table 1.
OMT Techniques for the COVID-19 Positive Pregnant Patient

Problem	Technique	Intended treatment effect	Modification for pregnancy
Increased laryngeal and facial edema	<ul style="list-style-type: none"> ■ Sinus drainage technique ■ Cranial bone lifts and effleurage ■ Soft tissue and myofascial techniques addressing secondary muscles of inspiration 	Relaxes the sternocleidomastoid and scalene muscles to aid in the drainage of the superficial and deep cervical lymph nodes. Allows improved respiration by relaxing the attachments to the manubrium and clavicle. Balances autonomics.	<ul style="list-style-type: none"> ■ Avoid prolonged treatment in the supine position. ■ Left uterine displacement: When supine, a rolled towel should be placed under the right hip to decrease caval compression, improve venous return, and maintain uterine blood flow and fetal oxygenation. ■ Perform in the seated position.
Increased sympathetic activity	<ul style="list-style-type: none"> ■ Occipito-atlantal decompression ■ Suboccipital release 	Decreases muscle spasms and restores upper cervical mobility while freeing the passage of the vagus nerve to balance autonomic tone by decreasing sympathetic and increasing parasympathetic tone.	<ul style="list-style-type: none"> ■ Left uterine displacement: When supine, a rolled towel should be placed under the right hip to decrease caval compression, improve venous return, and maintain uterine blood flow and fetal oxygenation.
Increased sympathetic activity Poor lymphatic and vascular drainage from the lungs	<ul style="list-style-type: none"> ■ Rib raising ■ Lumbar paraspinal inhibition ■ Thoracic pump 	Normalizes the sympathetic/parasympathetic nervous system. Decreases inflammatory cytokines.	<ul style="list-style-type: none"> ■ Left uterine displacement: When supine, a rolled towel should be placed under the right hip to decrease caval compression, improve venous return, and maintain uterine blood flow and fetal oxygenation.
Lymphatic congestion	<ul style="list-style-type: none"> ■ Thoracic inlet (necklace technique) 	Releases restriction of the thoracic duct, improving lymph drainage into the subclavian vein.	<ul style="list-style-type: none"> ■ Perform in the seated position.
Abdominal diaphragm dysfunction Impaired diaphragmatic movement especially in expiration	<ul style="list-style-type: none"> ■ Redoming of the diaphragm 	Decreases the hypertonicity of the diaphragm and restores its normal shape.	<ul style="list-style-type: none"> ■ Perform the technique in the supine position in the earlier half of pregnancy. ■ Perform in the seated position at later gestational ages.
Splenic congestion	<ul style="list-style-type: none"> ■ Splenic drainage 	Enhances the immune system by improving flow of lymph through the lymphatic system.	<ul style="list-style-type: none"> ■ Left lateral recumbent positioning.
Lower extremity congestion	<ul style="list-style-type: none"> ■ Pelvic diaphragm release 	Improves flow through both the lymphatic and circulatory systems. Decreases venous stasis to help prevent venous thromboembolism in the hospitalized patient.	<ul style="list-style-type: none"> ■ Perform in the supine position with a rolled towel placed under the right hip to minimize caval compression ■ Perform in the seated position. ■ If patient is already prone, treatment can be given without additional position modifications.

gestational age. We recommend that treatment be performed in the seated, semi Fowler's, or left lateral recumbent positions.

Providers should consider that patients may be asymptomatic carriers and should always wear PPE in the outpatient setting.

Conclusion

COVID-19 has not been definitively shown to cause increased mortality in pregnant patients compared with the general population. The physiological state of pregnancy may offer some protective benefits against COVID-19, while other coexisting pregnancy factors may predispose patients to a higher rate of hospitalization, ICU admission, overall morbidity, and increased likelihood of intubation. Due to potential ventilator shortages and intubation complications (such as increased likelihood of failure and rapid oxygen desaturation following apnea), additional treatments for COVID-19 should be considered in the pregnant population. OMT is safe and effective for many symptoms associated with COVID-19. Employing these techniques with appropriate modifications in pregnancy may prove to be increasingly beneficial. Further research is necessary to determine the efficacy of OMT in improving obstetric outcomes and decreasing morbidity and mortality for pregnant patients with COVID-19.

Author Contributions

All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article and revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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