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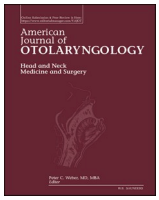

Impact of pregnancy on airway complications after intubation for COVID-19 infection: A case series☆,☆☆

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ABSTRACT

Coronavirus disease (COVID-19) is associated with severe acute respiratory illness, often requiring intensive care unit admission. Some patients require prolonged intubation and mechanical ventilation. Post-intubation laryngotracheal stenosis occurs in approximately four to 13 % of adult patients after prolonged intubation in the absence of COVID-19 infection. The rate of COVID-19 related post-intubation laryngotracheal stenosis may be higher. Of 339 pregnant patients with COVID-19, we identified seven who required intubation and mechanical ventilation. Four of the seven developed persistent airway complications, and laryngotracheal stenosis, the most severe, was present in three. Each patient had variations in duration of intubation, endotracheal tube size, re-intubation, presence of superimposed infections, and pre-existing comorbidities. We speculate that underlying physiologic changes of pregnancy in addition to the increased inflammatory state caused by COVID-19 are associated with an increased risk of post-intubation laryngotracheal stenosis. Otolaryngology physicians should have a low threshold for considering this pathophysiology when consulting on obstetric patients who have previously been intubated with COVID-19. Otolaryngologists can educate obstetricians when caring for pregnant patients who have laryngotracheal stenosis, especially those who may require emergency airway management for obstetric indications.

1. Introduction

Pregnant women were not spared from the coronavirus disease (COVID-19) pandemic [1]. Many struggled with the uncertainty of how the disease would affect them and their pregnancies. Up to 12 % of infected patients required intensive care unit (ICU) admission for a median of 17 days of mechanical ventilation [2]. These patients are also at high risk for re-intubation [3].

Laryngotracheal intubation can cause mucosal damage and tracheal wall necrosis, which poses a risk for the subsequent development of laryngotracheal stenosis (LTS). Risk factors for LTS include traumatic intubation, multiple intubations, and endotracheal tube size. The duration of intubation is the most important risk factor in adults and children [4]. Additional risk factors include female gender and elevated levels of estrogen [5].

Physiologic changes of pregnancy that affect the respiratory tract include mucosal capillary engorgement and subsequent increased mucosal edema [6]. These physiologic alterations coupled with COVID-19 infection may predispose pregnant patients to more severe outcomes [7]. Although the rate of COVID-19 related post-intubation LTS in pregnant patients has not been reported, it is possible that this complication is more common in pregnant in comparison to non-pregnant patients.

We describe four pregnant patients who required intubation and mechanical ventilation secondary to COVID-19 infection and were diagnosed with post-intubation LTS. IRB approval was obtained, exempt review #H-41624, to review these cases retrospectively, and CARE guidelines followed.

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2. Cases

Between February 1, 2020 and May 10, 2021, 339 pregnant women admitted to Boston Medical Center were diagnosed with COVID-19 infection. Seven of those women (2 %) required endotracheal intubation (Table 1). Four of those seven (57 %) subsequently developed LTS and are described below. All cases occurred before vaccination was widely available. Comorbidities and pregnancy management are included in Table 1.

2.1. Case 1

A 34-year-old G5P0 woman at 29 weeks gestation presented to the emergency department with fever, shortness of breath, chest pain, and cough and was diagnosed with COVID-19 via reverse transcriptase polymerase chain reaction testing (RT-PCR). She developed acute respiratory distress and required intubation. She was intubated for 15 days: first for eight days followed by self-extubation and then re-intubated for seven days. Her ICU course was complicated by pneumonia and urinary tract infections. Four months after discharge, she was re-admitted for persistent shortness of breath with mild inspiratory stridor. One year after discharge, she complained of persistent dyspnea and was diagnosed with subglottic stenosis measuring three to four millimeters (mm) in diameter. She experienced symptomatic relief after endoscopic excision and balloon dilation.

2.2. Case 2

A 32-year-old G2P1 woman at 27 weeks 3 days gestation presented to the emergency department with cough, fever, shortness of breath, and lethargy and was confirmed to be COVID positive via RT-PCR. She was subsequently intubated for three days, extubated, and re-intubated for eight days for persistent hypoxemia. Her re-intubation was complicated by superimposed MSSA pneumonia. Two weeks after discharge, the patient returned with biphasic stridor, sore throat, cough, and chest pain and was found to have 80 % circumferential narrowing of the subglottis two centimeters (cm) below her vocal folds. She was diagnosed with LTS and underwent laser excision with balloon dilation, while still pregnant, with some symptomatic relief. Her symptoms rapidly returned, and she has since required three procedures. One year after initial discharge, she continues to have 60 % SG and persistent difficulty breathing. She delivered a full term, healthy child.

2.3. Case 3

A 35-year-old G1P0 woman at 24 weeks gestation presented to the emergency department as a known COVID-positive patient with worsening cough, fever, chills, and shortness of breath. She was admitted to the ICU and intubated. Her ICU course was complicated by superimposed *Haemophilus influenzae* pneumonia. She was intubated for 19 days followed by a spontaneous self-extubation and re-intubated for three more days. She was stridulous on extubation and, upon further evaluation, was found to have pharyngeal and laryngeal edema. She had reduced epiglottis, esophageal, pharyngeal, and cricopharyngeal movement. Following discharge, re-evaluation revealed five to six millimeter glottic stenosis at the level of the intra-arytenoid tissue, limited abduction of the vocal cords, and inability to visualize the subglottis. She did not have any follow-up procedures and continues to have difficulty breathing while speaking and during activity.

2.4. Case 4

A 39-year-old woman at 34 weeks 3 days gestation presented to the emergency department with multiple symptoms and confirmed to be COVID-positive via RT-PCR. She had a progressive oxygen requirement, rapidly deteriorated and required intubation. Her ICU course was complicated by a superimposed MSSA pneumonia and inability to oxygenate, requiring extracorporeal membrane oxygenation. She was intubated for 18 days. After extubation, she was noted to have persistent stridor, laryngeal edema, supraglottic edema, limited abduction of the bilateral vocal folds, and laryngeal hoarseness. The patient was subsequently cared for elsewhere.

2.5. Cases 5, 6, 7

Did not exhibit respiratory complications

3. Discussion

Post-intubation LTS is rare with an estimated 4.9 cases per one million individuals per year in the general population [8]. Up to 5 % of non-pregnant adults with COVID-19 infection who required invasive ventilation developed symptomatic post-intubation LTS [9]. Risk factors for LTS include traumatic intubation, multiple intubations, large endotracheal tube size, and superimposed infection, with duration of intubation considered the most significant factor [4]. Additional risk factors include smoking, obesity, diabetes, female gender, and elevated levels of estrogen, which places pregnant patients at a higher risk of developing this complication [5]. We postulate that physiologic changes of pregnancy in patients infected with COVID-19 requiring intubation have a higher incidence of LTS than non-pregnant adults.

In this limited series, over 50 % of intubated pregnant patients at our institution were diagnosed with symptomatic post-intubation LTS. All patients had differences in duration of intubation ranging from 12 to 23 days, re-intubations, endotracheal tube sizes, and risk factors including obesity, diabetes, smoking, and hypertension. Shared characteristics amongst our patients include female gender, superimposed infection, and third trimester pregnancy physiology. This series is limited by its small sample size.

The hyperinflammatory state from COVID-19 likely compounds physiologic changes of pregnancy [10,11]. During pregnancy, capillary engorgement of the mucosa throughout the respiratory tract causes swelling of the nasal and oral pharynx, larynx, and trachea [6]. Estrogen increases transforming growth factor beta-1, which promotes extracellular matrix production, including the deposition of types one and three collagens and finally fibrosis [5]. Estrogen-mediated airway edema progresses throughout pregnancy, with the most severe edema occurring during the third trimester [12]. All of our patients with persistent airway complications were in their third trimester at the time of endotracheal intubation. Physiologic changes of pregnancy can be amplified by respiratory tract infections, worsening airway compromise, making pregnant patients more prone to scar formation and persistent stenosis.

We suspect that a combination of prolonged intubation, a heightened immune state, and physiologic changes to the respiratory system during pregnancy contributed to our patients' adverse outcomes. These cases highlight the importance of suspecting LTS in pregnant patients who have recovered from severe COVID-19. Given the variable nature of labor progression and acuity on the obstetric ward, it is important that otolaryngologists are aware of these patients at presentation.

4. Conclusion

As highlighted by these four cases, LTS is a significant complication of intubation that should be suspected in pregnant and postpartum patients recovered from severe COVID-19 who later present with breathing difficulties. The increased risk of LTS in this patient population may result from the synergism of the inflammatory damage cause by COVID-19 and respiratory physiologic changes of pregnancy. The symptomatic management of these pregnant patients included endoscopic excision and balloon dilations, which is similar to management for non-pregnant patients. Patients with LTS must be managed by a multidisciplinary group of physicians including otolaryngologists, obstetricians, and

Table 1
[a] Seven patients with COVID-19 infection required intubation at our institution.

Case #	Age	Gravidity and parity	Comorbidities	Pregnancy outcome	GA on admission	ETT size	Length of 1st intubation	Length of 2nd intubation	Superinfection	Steroids Administered	Proned?	Airway complications	Intervention
1	34	G5P0130	Obesity (BMI 33.4) Current smoker Asthma Pre-diabetes	Cesarean delivery while intubated	29 weeks 5 days	7.0 mm	8 days	7 days	Pseudomonal UTI MSSA pneumonia	Methylprednisolone sodium succinate 40 mg × 1 dose Methylprednisolone sodium succinate 80 mg × 1 dose	Yes	Laryngotracheal stenosis (LTS)	Laser excisions and balloon dilation × 2 with temporary relief
2	32	G2P1001	None (BMI 27.7)	NSVD post discharge	27 weeks 6 days	7.0 mm	3 days	9 days	MSSA pneumonia	None	Yes	LTS	Laser excision and balloon dilation × 3 with temporary relief (1 procedure while pregnant)
3	35	G1P000	Obesity (BMI 35.3)	Cesarean delivery post discharge	24 weeks 0 day	7.5 mm	20 days	3 days	*Haemophilus influenzae* *Enterococcus faecalis* UTI	Methylprednisolone 32 mg × 8 doses Dexamethasone 6 mg × 4 doses	Yes	LTS	None, persistent symptoms
4	39	G2P1001	Obesity (BMI 39.34)	Cesarean delivery while intubated	34 weeks 4 days	8.0 mm	18 days	N/A	MSSA pneumonia	Methylprednisolone 32 mg × 2 doses Dexamethasone 6 mg × 8 doses	Yes	Persistent laryngeal edema	None
5	26	G4P1021	Obesity (BMI 31.41) Current marijuana smoker	NVSD post discharge	30 weeks 0 days	7.5 mm	26 h	N/A	none	None	Yes	None	N/A
6	31	G2P1001	Obesity (BMI 33.27)	Cesarean delivery while intubated	31 weeks 1 day	7.5 mm	14 days	N/A	Pneumonia and sepsis with possible bacterial etiology	Methylprednisolone 40 mg × 2 doses Dexamethasone 8 mg × 1 dose	Yes	None	N/A
7	34	G3P2001	Obesity (BMI 31.4) Pre-eclampsia Hypothyroidism	Cesarean delivery prior to intubation[b]	34 weeks 1 day	7.0 mm	33 days	N/A	*Enterococcus faecalis* bacteremia	None	Yes	None	N/A

GA = gestational age, ETT = endotracheal tube, UTI = urinary tract infection, MSSA = methicillin-susceptible *Staphylococcus aureus*, BMI = body mass index, LTS = laryngotracheal stenosis, ROM = range of motion.

[a] These patients were cared for in the medical or surgical ICU. All patients were intubated with at least a 7.0 millimeter (mm) endotracheal tube. Neither the patient who was intubated for the longest (33 days) nor the shortest (26 h) amount of time had airway complications. Bolded cases (1–4) are those with airway complications.

[b] 1st intubation on post-Cesarean delivery day three.

anesthesiologists.

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