

Acute respiratory failure and mechanical ventilation in pregnant patient: A narrative review of literature

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Abstract

Physiological changes of pregnancy imposes higher risk of acute respiratory failure (ARF) with even a slight insult and remains an important cause of maternal and fetal morbidity and mortality. Although pregnant women have different respiratory physiology and different causes of ARF, guidelines specific to ventilatory settings, goals of oxygenation and weaning process could not be framed due to lack of large-scale randomized controlled trials. During the 2009 H1N1 pandemic, pregnant women had higher morbidity and mortality compared to nonpregnant women. During this period, alternative strategies of ventilation such as high-frequency oscillatory ventilation, inhalational of nitric oxide, prone positioning, and extra corporeal membrane oxygenation were increasingly used as a desperate measure to rescue pregnant patients with severe hypoxemia who were not improving with conventional mechanical ventilation. This article highlights the causes of ARF and recent advances in invasive, noninvasive and alternative strategies of ventilation used during pregnancy.

Key words: Intensive Care Unit, mechanical ventilation, physiological changes, pregnancy, respiratory failure

Introduction

Critical conditions warranting admission of pregnant patients to Intensive Care Unit (ICU) are relatively rare. The reported incidence varies between 0.4% and 16% of all ICU admissions. Acute respiratory failure (ARF) is the most frequent organ dysfunction associated with ICU admission and has dire maternal and fatal consequences if left untreated.^[1,2] Pregnant women have unique characteristics, and their management is challenged by the altered cardio-respiratory physiology, the presence of growing fetus, and diseases which are specific to pregnancy.^[3]

Methodology

A thorough and comprehensive literature search in medical databases (PubMed, Google Scholar, and Ovid MEDLINE)

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was performed with step-wise changes in relevant keywords (pregnancy, physiological changes, ICU, ARF, mechanical ventilation [MV]) without any data restriction including case reports, observational studies, randomized controlled trials (RCTs), and review articles. However, most of the evidence we found in the literature was in the form of case reports, case series, and review articles.

Physiological Changes in Respiratory System

Physiological changes during pregnancy occur due to hormonal effects, mechanical effects of the enlarging uterus, and increased metabolic demands of the fetoplacental unit. These changes, along with a decrease in functional residual capacity (FRC), and impairment in native immunity put parturients at higher risk of ARF with even a slight insult.^[4]

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Respiratory physiology differs in terms of changes in lung volumes, mechanics of ventilation and control of respiration.^[4,5]

With the progress of pregnancy, the circumference of the lower chest wall increases by 5-7cm with an increase in the anteroposterior and transverse diameters, resulting in widening of the costal angle from 68° to 103°.^[6] This compensates for the eventual elevation of the diaphragm. Lung compliance itself does not change during pregnancy, but chest wall and total respiratory compliances decrease by approximately 30%.^[6]

Major changes occurring in lung volumes are summarized in Table 1.^[4,5] As respiratory rate (RR) remains unchanged, tachypnea often is a sign of underlying pathology even in parturients. Increase in tidal volume (TV) accounts for mild respiratory alkalosis. The normal partial pressure of carbon dioxide (PaCO₂) during pregnancy is 27-34 mmHg. This is due to the stimulatory effects of progesterone on the respiratory center.^[7] The partial pressure of oxygen (PaO₂) ranges between 90 and 110 mmHg.^[4,5] Increase in the oxygen (O₂) demand coupled with a decrease in FRC causes smaller airways to close earlier when lung volume is reduced; putting pregnant patients at risk of rapid desaturation.^[8]

Delivery of O₂ to the fetus is affected by maternal delivery of O₂ to the placenta, and placental transfer. Frequent and severe episodes of hypoxia lead to low birth weight, intra uterine growth retardation (IUGR), preterm delivery, and increased perinatal morbidity and mortality.^[8] The literature recommends maternal PaO₂ >75 mmHg to protect the fetus from hypoxic injury.^[9] Fetal PaCO₂ of 65 mmHg or above is associated with detrimental effects. However, persistent respiratory alkalosis (pH >7.48) also causes uterine artery vasoconstriction and decreases fetal perfusion.^[10]

Obstetric Causes of Acute Respiratory Failure

In an epidemiological survey, Wanderer *et al.*^[2] found ARF to be the most frequent organ dysfunction (24.6%) present in obstetric patients at the time of ICU admission. The common causes are summarized in Table 2.^[9,11-17]

Hypertensive disorders

Hypertensive disorders during pregnancy are classified into four categories: Chronic hypertension, preeclampsia-eclampsia, preeclampsia superimposed on chronic hypertension, and gestational hypertension.^[18] It is the most common medical problem encountered during pregnancy, and also a common indication for ICU admission.^[2] Pregnancy-induced

hypertension (PIH) complicates 5-14% of all pregnancies and account for a maternal mortality rate (MMR) of 15-20%.^[19] Increases in hydrostatic pressure from hypertension and alterations in capillary membrane permeability, leads to pulmonary edema in nearly 3% of women typically after delivery, when plasma oncotic pressure is at its lowest.

Amniotic fluid embolism

Amniotic fluid embolism (AFE) or anaphylactic syndrome of pregnancy is a rare syndrome with high MMR, estimated to occur in 1-12/100,000 deliveries.^[20] It is now thought to involve an inflammatory anaphylactoid response to fetal antigens entering the maternal vasculature through disruption in the maternal-fetal barrier. This results in a clinical trial of increased pulmonary and/or systemic vascular resistance decreased left ventricular function and coagulopathy, resulting into cardio-respiratory failure and shock.^[21] Predisposing conditions include rapid labor, meconium-stained amniotic fluid, postterm pregnancy, eclampsia, cesarean section (CS), and placental abruption.^[22] Management is primarily supportive and is focused on the judicious use of intravenous fluids, hemodynamic monitoring, MV, and administration of blood products for correction of coagulopathy.^[21] MMR exceed 60% with classical presentation and increases to 90% if complicated by cardiac arrest. A significant number of survivors had neurologic sequelae from hypoxic-ischemic encephalopathy.^[21,23]

Air embolism

Air embolism can occur with normal labor, placenta praevia, criminal abortions, insufflation of the vagina during

Table 1: Changes in lung volumes and capacities during pregnancy

Total lung capacity decreases by 4-6%
Functional residual capacity decreases by 15-25%
Residual volume remains constant
Closing capacity remains unchanged
Minute ventilation increases by 20-45%
Tidal volume increases by 30-50%

Table 2: Causes of acute respiratory failure during pregnancy

Obstetric causes	Nonobstetric causes
Hypertensive disorder	Venous thromboembolism
Amniotic fluid embolism	Cardiovascular disease
Ovarian hyper-stimulation syndrome	Pulmonary artery
Acute fatty liver of pregnancy	Hypertension
Peripartum cardiomyopathy	Bronchial asthma
Chemical pneumonitis	Respiratory infection
Tocolytic induced pulmonary edema	Neuromuscular disorders
Septic abortion, chorioamnionitis, endometritis	Sepsis

gynecological procedures, and douching. The mechanism is attributed to entry of air into the sub-placental venous sinuses. A large amount of air collected in the right ventricle can lead to sudden death by blocking the outflow tract. Entry of air into the pulmonary vasculature can cause pulmonary artery hypertension (PAH), right heart failure (RHF) and pulmonary embolism (PE).^[24]

Ovarian hyperstimulation syndrome (OHSS)

OHSS is an iatrogenic, life-threatening complication of ovarian stimulation which is being increasingly recognized due to the higher number of women undergoing assisted reproductive techniques. It is associated with the use of gonadotropins, or occasionally clomiphene citrate. The increase in capillary permeability is believed to be the pathognomic sign of this syndrome leading to complications such as ascites, hydrothorax, and anasarca. The clinical features include rapid weight gain, abdominal pain, nausea, vomiting, breathlessness, thromboembolism, hepatic, and renal failure. About 1-2% of women develop a severe form of OHSS warranting ICU admission and aggressive treatment with crystalloids, colloids, albumin, loop diuretics, anticoagulants, cabergoline, and gonadotropin-releasing hormone antagonist. MV is required to manage PE, acute respiratory distress syndrome (ARDS), intra-alveolar hemorrhage and sepsis.^[25]

Acute fatty liver of pregnancy

It is a rare clinical entity with an incidence of 1 in 13,000^[26] affecting pregnant women in their 3rd trimester. It can lead to hepatic failure, encephalopathy, ARDS, coagulopathy, diabetes insipidus and hypoglycemia. It is histologically and clinically similar to Reye's syndrome, a disease of microvesicular fatty infiltration caused by abnormal oxidation of mitochondrial fatty acids. Liver biopsy is the gold standard diagnostic test, but given the potential for coagulopathy, a biopsy should only be used when the diagnosis is unclear. No specific management is available for this fulminant disorder. However, successful orthotopic liver transplant in a woman with acute fatty liver of pregnancy has been reported.^[27]

Peripartum cardiomyopathy

It is a rare form of serious, potentially life-threatening heart disease of uncertain etiology occurring in 3rd trimester of pregnancy or up to 5 months after delivery.^[28] The reported incidence is very low (1 in 15,000 deliveries) with an MMR of 20-50%.^[29] Recent data have shown that unbalanced peri/post-partum oxidative stress leads to proteolytic cleavage of the hormone prolactin causing pro-apoptotic, and inflammatory changes leading to cardiomyopathy.^[28] Restricted sodium diet, loop diuretics, vasodilators, inotropes, beta-blockers, angiotensin converting enzyme inhibitors, immunoglobulins, ventricular assist devices, and heart transplantation have been used for the management.

Chemical pneumonitis

Mendelson's syndrome occurs secondary to aspiration of gastric contents following induction of general anesthesia or in the early postoperative period, resulting in ARDS and PE. Parturients are at high risk of aspiration due to decreased tone of the lower gastro-esophageal sphincter, increased intra-gastric pressure, and decreased gastric emptying. Few hours after aspiration, there can be hypoxia, cyanosis, dyspnea, tachycardia, and shock. There can be bloody, frothy sputum with marked pulmonary congestion. PE may supervene, with a rapidly deteriorating course resulting in death.^[30] The risk may be reduced by administering a nonparticulate antacid (e.g., sodium citrate) or an H₂-antagonist like ranitidine and by performing rapid sequence induction (RSI). However, the use of high volume of antacid can itself induce vomiting and the effectiveness of RSI has been questioned recently.^[31] Increase in the use of regional anesthesia has significantly decreased the incidence of Mendelson's syndrome.

Anemia

Iron deficiency and malnutrition are important causes of anemia in developing countries. Severe anemia of pregnancy is associated with poor outcome. It can lead to palpitations, tachycardia, breathlessness, increased cardiac output leading to increased workload resulting in cardiac de-compensation and failure. Increased incidence of preterm labor (28.2%), preeclampsia (31.2%), and sepsis have also been associated with anemia.^[32]

Nonobstetric Causes of Acute Respiratory Failure during Pregnancy

Venous thromboembolism

Pulmonary venous thromboembolism (VTE) complicates 0.05-0.3% of all pregnancies and is the leading cause of maternal death in the developed world.^[33,34] Hypercoagulation and venous stasis occur as physiological changes during pregnancy, putting pregnant women at higher risk (relative risk of 4.3) for PE than compared to nonpregnant women.^[35] Risk factors include heart disease, age >35 years, CS, sickle cell anemia, diabetes, smoking, multiple pregnancy, obesity, oral contraceptives, hormonal replacement therapy, and personal or family history of VTE.^[34]

Echocardiography, ventilation-perfusion scan, spiral computed tomography pulmonary angiography, blood gases, and venous Doppler of lower limbs may help to reach the diagnosis. Therapeutic anticoagulation with unfractionated or low molecular weight heparin (LMWH) should be initiated in the absence of contraindications.^[36] Intravenous unfractionated heparin is the initial treatment of choice as it does not cross

the placenta and has a short half-life so that it can be titrated before vaginal delivery or CS. LMWH is the agent of choice in the antenatal period. Warfarin is, however, safe in breastfeeding mother and can be commenced between 5 and 7 days postdelivery. Treatment with anticoagulants should ideally be continued for 3-6 months. Although experience with thrombolytic therapy in pregnancy is limited, use of such agents may be lifesaving in patients with hemodynamic compromise.^[36,37] Use of temporary vena caval filters, percutaneous mechanical clot fragmentation, compression stockings and cardiopulmonary bypass with surgical embolectomy have also been reported.^[36]

Pulmonary artery hypertension

PAH during pregnancy carries high mortality (30-50%) irrespective of its etiology.^[38] Severe PAH precipitates RHF resulting in decreased cardiac output and sudden death. Echocardiography is the most useful imaging modality. Epoprostenol, an intravenous prostaglandin is often considered as the first-line therapy.^[39] Phosphodiesterase-5 inhibitors such as sildenafil has also been used safely during pregnancy.^[40] Endothelin receptor antagonists such as bosentan and sitaxsentan have teratogenic effects, and hence, should be avoided. Even though newer therapies have emerged in the last decade for the management of PAH, significant risk still persists and current guidelines recommend that pregnancy is best avoided or terminated in women with severe PAH of any cause.^[41] Hospitalization at 20 weeks of gestation with close monitoring, bed rest, anticoagulants, pulmonary vasodilators, and joint management by obstetricians, cardiologists, and anesthesiologist is recommended for patients who wish to continue their pregnancy.^[41]

Bronchial asthma

The prevalence of bronchial asthma varies between 3% and 12% of all pregnancies and approximately 6% of patients get hospitalized due to acute exacerbation.^[42] Major causes worsening the severity include nonadherence to medications and viral infections leading to IUGR, preterm labor, preeclampsia, oligohydramnios, and pneumonia.^[43] Schatz *et al.*^[44] found that obstetric patients whose bronchial asthma was actively managed had similar maternal and fetal outcomes as compared to those without bronchial asthma. Inhaled bronchodilators and corticosteroids can be safely used during pregnancy as they are less likely to cross the placenta and affect the fetus. Bakhireva *et al.*^[45] examined the effect of inhaled and systemic corticosteroids, and beta-2 agonists on fetal growth. The mean birth weight of infants born to mothers treated with systemic corticosteroids resulted in a deficit of about 200 g compared with controls and exclusive beta-2 agonist users and no increased incidence of small for gestation age. The authors concluded that use of beta-2 agonists and/

or inhaled corticosteroids during pregnancy does not impair fetal growth, whereas systemic corticosteroids have a minimal effect which should be weighed against the necessity to control severe asthma. However, theophylline is not usually preferred during pregnancy.

Peak expiratory flow rate (PEFR) does not change with pregnancy and bedside tools (Wright's spirometer and Debono's whistling tests) can be used as simple diagnostic and prognostic indicators.^[46] Clinical parameters such as tachycardia (heart rate >120/min), tachypnea (RR >30/min), use of accessory muscles of respiration, excessive sweating, orthopnea, impaired consciousness, pulsus paradoxus, and PEFR <120 L/min indicate the need for hospitalization.^[47] Initial management consists of repeated administration of beta-2-agonists, corticosteroids, and supplemental O₂. Rising levels of PaCO₂ (including normalization in a previously hypocapnic patient), exhaustion, impaired consciousness, hemodynamic instability and refractory hypoxemia warrants ICU admission and MV. Use of helium in combination with O₂ to facilitate gas exchange and to limit peak inflating pressures has also been reported.^[48]

Restrictive lung disease

Women with mild to moderate restrictive lung disease (RLD) tolerate pregnancy reasonably well, but many have a premature delivery. Patients with severe RLD (vital capacity <1 L/min) should be advised to avoid pregnancy or consider a therapeutic abortion. If patient wishes to continue with the pregnancy, optimal medical management of the underlying disease and delivery by CS should be considered. The postoperatively patient may require MV.

Trauma

Trauma has become one of the most frequent causes of maternal death (36%) in the developed world. Road traffic accidents account for 70% of all traumas in pregnant patients.^[49] The principle guiding therapy must be that resuscitating the mother will resuscitate the fetus. The commonest obstetric problem caused by trauma is uterine contractions. Placental abruption after trauma occurs in 2-4% of minor accidents and in up to 50% of major injuries.^[50] Left lateral tilt at the earliest opportunity should precede primary survey. The patient may require MV for tension pneumothorax, lung contusions, flail chest, and hemodynamic instability.

Respiratory infection

The organisms causing bacterial pneumonia during pregnancy are the same as those found in the nonpregnant state. Pneumococcal pneumonia followed by mycoplasma pneumonia are the usual organisms isolated. In hospitals, nosocomial infection with Gram-negative organism must be

considered. Varicella pneumonia is associated with a high mortality of 45% during pregnancy compared with 20% in nonpregnant patients.^[51] Among the fungal infections, *Coccidioides immitis* can affect 1 in 1000 pregnant women.^[51] The patient may remain asymptomatic or develop transient pneumonitis. In a retrospective study, Benedetti *et al.*^[52] reported an MMR of 40/1000 deliveries due to antepartum pneumonia.

During the 2009 H1N1 pandemic, pregnant women had higher morbidity and mortality compared to nonpregnant women. There have also been reports of increased risk of miscarriage, birth defect, and preterm delivery.^[15,53] The complications were more frequent with advanced gestation.^[54] In addition to antivirals and antipyretics, respiratory support may be required with supplemental O₂, MV and alternative strategies of ventilation. H1N1 influenza per se is not an indication for delivery; nevertheless, CS was often performed to improve maternal oxygenation and respiratory function rather salvage a compromised fetus.

Acute respiratory distress syndrome

ARDS can result from or modified by an obstetric factor [Table 3].^[9] The reported incidence varies between 1 per 6000 and 10,000 deliveries, occurring primarily in the 3rd trimester.^[9,55,56] Perry *et al.*^[57] found an MMR of 30-50% and perinatal mortality of 20-25%. Arterial blood gas (ABG) criteria for intubation may vary depending on the gestational age. Inability to maintain a PaO₂ of 70 mmHg or SpO₂ of 95% with conservative therapy suggests respiratory compromise and warrants intensive therapy.^[58] High rates of fetal death, spontaneous preterm labor, and fetal heart rate (FHR) abnormalities are reported in neonates born to these pregnant women.^[51]

Pulmonary edema

Acute PE in pregnant women is an uncommon but life-threatening event. Incidence varies from 0.08% to 3%^[59,60,61] [Table 4].

Iatrogenic fluid overload is the most common cause of PE as pregnant women already have increased blood volume and are vulnerable to volume overload. Sodium and water retention secondary to oxytocin administered during delivery and preexisting cardiac abnormalities such as valvular heart disease, congenital heart disease including Eisenmenger syndrome, coarctation of the aorta, and cardiomyopathy further precipitates the condition.

Tocolytics are used to delay preterm labor if it occurs between 24 and 34 weeks of gestation and use of glucocorticoids is

likely to enhance the lung maturity, provided there is no contraindication to their use, and where a delay in delivery of the newborn is likely to improve neonatal outcome. The incidence of tocolytic therapy induced pulmonary edema is approximately 1 in 400 patients receiving beta-adrenergic agents.^[13] It can occur during the treatment or up to 12 h after the discontinuation of the drug. These adrenergic drugs cause vasodilatation and tachycardia resulting in hypotension. Treatment with intravenous fluids predisposes already fluid overloaded patient into PE. By acting on the beta-receptors in the proximal tubules of the kidney, these drugs stimulate renin and antidiuretic hormone synthesis resulting in sodium and fluid retention. Patients on tocolytic treatment also receive steroids to accelerate fetal lung maturation, and their mineralocorticoid activity aggravates the condition.^[13] Treatment consists of discontinuation of tocolytic drug therapy, administration of loop diuretics and supplemental O₂. Use of both noninvasive and invasive MV has also been reported.^[62]

Mechanical Ventilation

During the initial stages of maternal decompensation, the best support for the fetus is to maintain a nonhostile intrauterine environment. The physiological changes of pregnancy like an increase in O₂ demand, respiratory alkalosis, a decrease in FRC and decrease in respiratory compliance should be taken into account. The presence of mucosal edema, capillary engorgement, and increase in breast size, warrant a 0.5 mm smaller endotracheal tube compared to nonpregnant women of similar height and age. Start with a 7 mm endotracheal tube for the average-size pregnant woman. Although a PaO₂ of 55 mmHg and SpO₂ of 88% would be tolerated in the general population, adequate fetal oxygenation requires a PaO₂ of 70 mmHg, which corresponds to a maternal SpO₂

Table 3: Causes of acute respiratory distress syndrome during pregnancy

Direct obstetric causes	Causes modified by pregnancy
Hypertensive disorders	Gastric aspiration
Amniotic fluid embolism	Pneumonia
Placental abruption	Pyelonephritis, pancreatitis
Retained placental products	Trauma
Septic abortion,	Massive blood transfusions
chorioamnionitis, endometritis	

Table 4: Causes of pulmonary edema

Tocolytics
Hypertensive disorders
Amniotic fluid embolism
Iatrogenic fluid overload
Cardiac disease (cardiomyopathy, ischemic heart disease)
Peripartum cardiomyopathy

of about 95%.^[9] Clearance of fetal PaCO₂ by the placenta requires a gradient of approximately 10 mmHg.^[10] Limited data suggest that PaCO₂ levels of 45-55 mmHg is reasonable in the later part of pregnancy.

Noninvasive ventilation

Noninvasive ventilation (NIV) has been successfully used during pregnancy to treat ARF resulting from bronchial asthma, sickle cell anemia, all-trans-retinoic-acid syndrome, tocolytic induced pulmonary edema, influenza, community acquired pneumonia, ARDS, etc.^[10,63-66] It avoids the potential complications of endotracheal intubation, and that of the drugs used for sedation. Usually, an inspiratory pressure of 12-15 cmH₂O and an expiratory pressure of 5-8 cmH₂O are used.^[66] Its implementation under close monitoring would shorten hospitalization and ICU stay. However, decreased tone of the lower gastroesophageal sphincter, increased intragastric pressure and decreased gastric emptying put parturients at higher risk of gastric aspiration. Positive pressure ventilation through face mask may lead to gastric distension and vomiting.^[3] Therefore, NIV should be reserved for patients who are alert and conscious, have protective airway reflexes, good respiratory drive, and stable hemodynamics with no severe acid-base disturbances.

Invasive ventilation

Specific guidelines on ventilatory settings, goals of oxygenation and weaning process are still lacking during pregnancy.^[67] Initiation of MV in a pregnant patient with ARDS should follow the guidelines of the ARDS network study.^[68]

If respiratory acidosis (PaCO₂ >65 mmHg) persists despite high RR, the TV can be increased as long as plateau pressure remains <30 cmH₂O.^[69] Though it could be argued that decrease in the chest wall compliance should allow for an increase in the plateau pressures limit, Campbell *et al.*^[69] were of the opinion that ARDS network guidelines should not be altered, as it is the lung compliance which becomes the major determinant of total respiratory compliance rather than the effect of pregnancy on chest wall compliance.

During the influenza pandemic of 2009, Pollock *et al.*^[70] compared the provision of MV to pregnant/postpartum women with a nonpregnant matched control group. They studied 36 cases and 38 controls. There were no differences in the preintubation and postintubation ABG values apart from a lower PaCO₂ and bicarbonate levels in cases. Initial ventilator settings including mode, TV, and RR demonstrated no differences between the cases and controls. MMR did not significantly differ between the two groups (52.6% vs 48.3%).

Alternative strategies of ventilation

Extra corporeal membrane oxygenation (ECMO)

Early initiation of ECMO is recommended if ARF with refractory hypoxia is encountered in a pregnant woman. It saves the life of the mother but exposes the fetus to complications of systemic heparinization and extracorporeal circulation. The decision to perform CS while the patient is on ECMO is not easy due to the increased risk of thrombosis from the required duration of heparin discontinuation and risk of bleeding if heparin infusion is continued. Nair *et al.*^[71] retrospectively studied 12 critically ill pregnant and postpartum women suffering from severe ARDS during the H1N1 pandemic who required ECMO therapy. The technical challenges, efficacy, complications and maternal/fetal outcomes were evaluated. ECMO circuit related complications were rare, circuit change was needed in only two cases, and there was no sudden circuit failure. However, bleeding was common, leading to large volumes of blood cell transfusion and was the main cause of mortality.

Prone position

In addition to usual care, pregnant women require greater emphasis on avoiding any external abdominal pressure, continuous fetal monitoring and highly dedicated supporting staff. In addition prone positioning is logistically challenging even in nonpregnant patients and benefits are short and do not last once the position is changed to supine. However, case reports of successful use of prone ventilation in pregnancy with ARDS are reported.^[72]

High-frequency oscillatory ventilation

It is a lung protective form of ventilation which was used as a rescue therapy in up to 12% of patients with H1N1 associated ARDS who initially showed no signs of improvement with antivirals and conventional MV.^[73]

Nitric oxide

It is not known whether inhalational of nitric oxide (iNO) can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.^[74] It is also not known whether NO is excreted in human milk or not and is not approved for use by Food and Drug Administration (FDA). However, Michael *et al.*^[75] reported a case of successful use of iNO of up to 40 parts per million for 2 days in a pregnant patient with severe ARDS.

There are few case reports supporting the use of alternative strategies of ventilation like high-frequency oscillatory ventilation, iNO, prone positioning, and ECMO during the 2009 pandemic of H1N1 influenza as a desperate measure to rescue pregnant patients with severe hypoxemia who were not improving with conventional MV.

Weaning

Weaning parameters for pregnant patients are not well-established, but it seems reasonable to follow the same guidelines as for nonpregnant patients.^[76]

Sedation and Paralysis

RCTs evaluating drugs for providing long-term sedation, analgesia, and neuromuscular blockade are lacking in pregnancy. Benzodiazepines freely cross the placenta and may accumulate in the fetus. Use of diazepam in early pregnancy has been linked with a small risk of cleft lip and palate.^[77] Midazolam and lorazepam appear to cross the placenta to a lesser degree than diazepam, although the clinical significance is unknown.^[78] There are no large data on the use of dexmedetomidine during pregnancy. Few case reports described its use for sedation near term and all patient's required CS.^[79] Higher doses (0.5 µg/kg/h) or prolonged duration of infusion lead to fetal bradycardia. Propofol has been assigned to pregnancy category-B by the FDA. It rapidly crosses the placenta and distributed into fetal circulation. Higher doses (2.8 mg/kg) can result in low Apgar scores, muscle hypotony, and depressed neuromuscular activity. But by large no difference was found in the Apgar scores of infants exposed to propofol during CS. Animal studies failed to reveal fetal harm or impaired fertility. There are no RCTs conducted in human pregnancy and no data on the prolonged use of propofol is available during pregnancy. Congenital malformations have not been reported with the use of opioids such as morphine and fentanyl. Nondepolarizing neuromuscular blocking agents freely cross the placenta, but found to have no clinical effect on the fetus in the short term.^[78]

Fetal Monitoring

During prolonged MV, it is reasonable to measure and record daily FHR tracing, weekly umbilical artery Doppler and every fortnight ultrasound scan for fetal growth and monitoring. When gestation has progressed enough for delivery by CS, amniocentesis may be helpful to determine fetal maturity. If early delivery is not an option, the best course is to focus on optimizing the health of the mother and not on minute-to-minute variations in FHR.

Radiological investigations like chest X-ray are routinely required for the assessment and management of ventilated pregnant patients. A single chest X-ray results in 60 millirads of exposure. Although there is a potential risk of exposing the fetus to radiation, shielding the abdomen with lead and using a well-collimated X-ray beam can reduce fetal exposure.^[80]

Radiation exposure >0.05-0.5 Gy (5-50 rads) leads to teratogenicity and fetal demise in 1st trimester, gross congenital malformation and mental retardation in 2nd trimester and depletion of cell population in 3rd trimester.^[81]

Ethical and Social Issues

Prolonged MV during pregnancy entails significant ethical and management considerations. Even after brain death, few mothers can carry on their pregnancy until term. Hence, end-of-life care decisions are difficult to make with a viable fetus and may understandably be postponed until delivery. Tomlinson *et al.*^[82] noted that early delivery of the fetus reduces maternal O₂ requirement by an average of 28% within 24 h. Case reports of prolonged support exceeding 100 days with the successful delivery of a viable fetus are reported in the literature.^[83] Preservation of utero-placental blood flow due to the absence of autoregulation of the uterine vasculature is the priority. In the systematic review done by Esmaeilzadeh *et al.*^[84] organ donation from the brain-dead mother was carried out in ten patients with an excellent 1 year graft survival. Conducting RCTs on the mother during pregnancy also involve social and ethical issues and hence are difficult to undertake.

Conclusion

Though pregnant patients have different respiratory physiology and different causes of respiratory failure, guidelines specific to MV in pregnant patients could not be framed and in general the principles of MV that are used for nonobstetric patients are also followed in pregnant patients. Selection of drugs should take into account of its possible teratogenic effects and list of safe drugs should be available in obstetric ICU. Fetal monitoring is an essential part of ICU care and obstetric consultation should be sought on the safety of continuation of pregnancy and method of delivery at the earliest.

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Conflicts of interest

There are no conflicts of interest.

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