

ANESTHESIOLOGY™ 2014

OCTOBER 11-15 | NEW ORLEANS, LA

Session: L081
Session: L147

Critical Management of a Parturient With Influenza Progressing to ARDS

Vernon H. Ross, M.D.

Wake Forest University School of Medicine, Winston-Salem, NC

Disclosures: This presenter has no financial relationships with commercial interests

Stem Case and Key Questions Content

A 28 year old pregnant female G5 P 1 at 26 weeks gestation presents to labor with cough, congestion, fever chills and shortness of breath.

What is the differential diagnosis of shortness of breath in a parturient?

What changes in respiratory physiology can be expected during pregnancy?

What are the expected changes in cardiovascular physiology during pregnancy?

Her vital signs at presentation are Temp 101.7° Fahrenheit (F) Blood Pressure (BP) 139/77 mmhg Heart Rate (HR) 120 beat per minute Respiratory Rate (RR) 26 breaths per minute (bpm) Fetal Heart Rate (FHR) 160's beats per minute. The Past Medical History includes chronic diabetes mellitus, and chronic hypertension. She has a history of a low transverse cesarean section. Influenza swabs are taken and the patient is started on Oseltamivir po 75mg BID, Acetaminophen po for fever and supplemental oxygen 4 liters/min via nasal cannula?

How does influenza present? How is influenza treated? Why do pregnant patients with influenza have a high risk of respiratory failure?

What conditions may be associated with an increase risk of morbidity and mortality in the parturient infected with influenza?

Respiratory symptoms progress to shortness of breath (SOB), tachypnea, tachycardia and decreasing O₂ saturation. Vital Signs are Temp 100° Fahrenheit, HR 110-120 bpm RR 20-28 bpm. Heart examination showed sinus tachycardia with no murmur. Lung examination reveals bibasilar rales. An arterial blood gas reveals pH 7.43, pCO₂ 35, pO₂ 63 with an O₂ saturation of 92%. The Hgb is 8.6 g/dL and a WBC is 16,000 thou/mcL. Chest x-ray showed no acute changes. She is treated with nebulized Albuterol. An infectious disease consult is obtained and she is started on Ceftriaxone 2g qd iv and Azithromycin 500mg qd iv and transferred to the ICU.

What are the most common reasons for ICU admissions for obstetrical patients?

How should the care be organized and coordinated when a parturient needs critical care?

What are the infectious and isolation considerations for the parturient with influenza?

The patient is on non-invasive Bi-level positive airway pressure (BiPAP) with settings of 16/5 cm H₂O at 60% FiO₂ and a repeat blood gas indicate deterioration of her pulmonary status: pH 7.44 pCO₂ 34 mm Hg and pO₂ 50 mm Hg. The patient's physical exam reveals increased work of

ANESTHESIOLOGY™ 2014

OCTOBER 11-15 | NEW ORLEANS, LA

breathing with the use of accessory muscles, and tachypnea. Diffuse rales are heard bilaterally. It is decided that intubation and mechanical ventilation is warranted.

What are the unique challenges and problems presented by the parturient requiring intubation? Is there any different equipment that is needed for intubation?

A Glidescope is available during intubation. The patient is intubated with a 7.5 mm endotracheal tube after rapid sequence induction with 200 mg Propofol, 100 mg of succinylcholine iv. A MAC 3 blade is used and a grade I airway view is observed. After intubation, there is positive ETCO₂ detected with capnography. Equal bilateral breath sounds are heard. Frothy foam is suctioned from the endotracheal tube and the patient is manually ventilated with an ambu bag with 20 cm H₂O positive end expiratory pressure (PEEP) to O₂ saturation of 100%.

What types of mechanical ventilation settings are optimal in the pregnant patients with severe respiratory insufficiency? In severe respiratory insufficiency can extracorporeal membrane oxygenation (ECMO) be used?

The patient is placed on assist control ventilations with a tidal volume of 7 ml/kg, rate of 16 breath per minute and 20 cm H₂O of peep initially and FiO₂ to maintain saturation of 96%. The FHR's continue to do well in the 130- 140 bmp range.

What drugs can be used to maintain sedation while the parturient is on ventilatory support? What effect does obstetric medication have on the critically patient? Should fetal heart tracings be monitored? Does delivery of the fetus improve the outcome of pregnant patients with severe respiratory insufficiency?

Model Discussion Content

Differential Diagnosis

The differential diagnosis for shortness of breath in the parturient includes preeclampsia leading to pulmonary edema, pulmonary embolus, congestive heart failure and influenza or other respiratory infections.

Physiology

Pregnant patients have many respiratory changes that put them at increased risk for respiratory compromise during critical illness. Minute ventilation increases approximately 30%, primarily due to an increase in tidal volume. The PaCO₂ drops to 28 -32 mm Hg, and with renal compensation, the arterial pH is maintained between 7.40 and 7.45. An increase in PaCO₂ above 40 mm Hg reflects significant respiratory compromise. PaO₂ is normally slightly increased to 100 to 105 mm Hg. Pregnant patients have a diminished capacity for respiratory compensation to metabolic acidosis. The functional residual capacity (FRC) is reduced by 10% to 20% because of elevation of the diaphragm. Oxygen consumption increases by 20% to 33% due to increases in maternal metabolism and to meet the demands of the fetus.

Blood volume increases 35-45%, and plasma volume increases by 50%. Cardiac output increases 30-50% due to increases in both stroke volume (~30%) and heart rate (~15%).

Systemic vascular resistance decreases by 20%. Vena caval compression is caused by the occlusion of the aorta and vena cava due to the gravid uterus (especially after 28 weeks). It may cause a decrease in venous return, stroke volume, and cardiac output. When maternal circulation is compromised and compensatory vasoconstriction occurs, uteroplacental perfusion can be reduced leading to fetal hypoxia.¹

Influenza and Pregnancy

The incubation period of influenza is 1 to 4 days. Symptoms include cough, fever, malaise, headache, and myalgias. Other respiratory signs such as rhinitis, sore throat, and nasal congestion can occur. This congestion can progress down to the lungs and culminate in a viral pneumonia. Studies of the 2009 H1N1 pandemic demonstrate that pregnant women with influenza are at increased risk of serious illness and death. The risk of influenza complications appears to be higher in the second and third trimester than in the first trimester. Pregnant women in all 3 trimesters were at increased risk of influenza associated complications.^{2, 3, 4, 5} The mainstay of treatment is the neuraminidase inhibitor antiviral agent Oseltamivir. It is used against influenza A and B for prophylaxis, high risk patients, and in complicated cases.^{6, 7} This drug is a category C drug. The placental transfer of its metabolites appears to be low, and the incidence of adverse maternal or fetal outcomes after exposure is not higher than background rates. The incidences of spontaneous abortion, therapeutic abortions, and preterm deliveries are 6.1%, 11.3%, and 2.1%, respectively.⁸

Parturients suspected of having influenza have a better prognosis the earlier they are treated. When given Oseltamivir within 48 hours of the onset of symptoms, parturients have decreased mortality (only 0.5%) compared to those that receive treatment between days 3 and 4 days. In contrast, this intermediate group had a mortality rate of 5%. The use of antivirals also lowers the ICU admission rates among influenza infected women. 68% of patients receiving early antiviral vs. 79% receiving intermediate treatment were hospitalized. 9% receiving early treatment vs. 23% intermediate treatment required admission to the intensive care unit (ICU). 5% receiving early treatment vs. 17% receiving intermediate treatment required mechanical ventilation.² Pregnant women whose treatment is delayed even further, beyond 4 days, are more than 50 times as likely to die compared to the early treatment group.

Oseltamivir is extensively metabolized by the placenta, leading to undetectable levels even at treatment doses above recommended dosing strategies.² For more severe cases, supplemental oxygen therapy is added. This oxygen demand may progress to a need for non-invasive ventilation or full mechanical ventilation depending on the severity of compromise.

There is diminished cell-mediated immunity in the parturient. Maternal lymphocytes exhibit a decreased response to antigen stimuli. There is also a decrease in natural killer cell activity.^{9,10} This puts the pregnant patients at an increased risk of serious respiratory compromise if influenza is not treated. Data from seasonal influenza seems to demonstrate that pregnant women are at a higher risk for hospitalization than women a year before pregnancy.¹¹ During the 2009 Pandemic, in the US, pregnant women accounted for approximately 1% of the

population; yet, they accounted for 5% of US deaths from influenza A H1N1.²

30% of parturients that progressed to more severe disease had additional risks factors. Parturients with asthma (22.9%), obesity (13%), diabetes mellitus (6.7%), anemia (3.5%), and hypertension (3%) are at higher risk of developing complications and severe respiratory insufficiency from an influenza infection. Underlying conditions were more common among women hospitalized (55.3%), admitted to the ICU (62%), and those that died (78.3%).³

ICU Admission

Parturients that are admitted to the ICU are those who need circulatory or pulmonary support. Hemorrhage and hypertension are the most common causes of ICU admission for parturients. Other causes include patients who require cardiovascular support, such as treatment with vasopressors, pulmonary artery catheterization (insertion, maintenance, and interpretation), arterial lines, and patients' with abnormal electrocardiographic findings requiring intervention. Any patient who needs increasing ventilatory support would benefit greatly from being monitored and managed in an intensive care setting. Patients' requiring airway maintenance and endotracheal intubation definitely need critical care management.^{1,12}

A multidisciplinary care team (obstetrician, intensivist, anesthesiologist and neonatologist) should assess the anticipated course of the patient's condition, including possible complications and set parameters for delivery if appropriate. The plan should be clear to the medical team and to the patient herself. Plans for delivery should be made and reevaluated during the course of the parturient's care. A delivery plan must include the preferred location of delivery and the preferred mode. Prior to the parturient being in active labor, the ICU setting is the best place to meet critical care needs. If vaginal delivery occurs, there should be availability of all team members. The critical care staff is generally unfamiliar with obstetric interventions and management. A team approach is necessary for optimal care.^{1,12}

Transmission of the influenza virus is primarily by droplets and contact with respiratory secretions. Patients suspected of having influenza should be placed on droplet isolation, and healthcare workers should wear a surgical mask, face shields, eye protection, gowns, and gloves as the appropriate protective equipment.¹³

Intubation

In pregnancy, slowed gastrointestinal motility, progesterone mediated loss of lower esophageal sphincter tone, and higher intra-abdominal pressures all increase the risk of pre-intubation aspiration. The airway mucosal edema and friability can obscure visualization of the vocal cords. This increases the risk of trauma and bleeding during intubation. Failed intubation has been reported to be increased 8-fold during pregnancy compared to the general population.¹⁴ Difficult laryngoscopy and failed intubation are more common in the parturient and is associated with higher mortality. The increased oxygen consumption and decreased FRC can leave very little margin for error.

The airway differences in the parturient may require smaller endotracheal tubes than are used in non-pregnant adults. Adjunctive equipment that is recommended for the management of the obstetrical patients' airway includes intubating laryngeal mask airway (LMA), lighted stylet, glide scope, or fiberoptic endoscope.^{15,16} Because of the decreased FRC, intubation may need to be considered early if the parturient is not improving with non-invasive ventilator techniques (i.e., O₂ via nasal cannula, non-rebreathing mask, BiPAP). Rapid sequence induction should be utilized if patients are to be rendered unconscious for intubation. Propofol and ketamine have been used safely in the parturient. Succinylcholine for muscle relaxation facilitates the intubation and is safe.

Mechanical Ventilation

Many clinicians will use an assist /control mode of ventilation using a low tidal volume (7-8 ml/kg body weight) and a rate to maintain good minute ventilation and peak airway pressures < 40 cm H₂O. A small amount of PEEP is used to help decrease FiO₂ but maintain adequate oxygen saturations. Tidal volumes should be set at the non-pregnant predicted body weight. Severe barotrauma is a risk with higher airway pressures. However, because chest wall compliance is reduced in near term patients and trans-pulmonary pressures may be elevated slightly, higher airway pressures may be tolerated. Severe respiratory alkalosis should be avoided because this can promote uterine vasoconstriction and adversely affect uterine blood flow.^{1,17,18} High PEEP can raise intra-thoracic pressure and may restrict venous return to the thorax, negating adaptive high cardiac output seen in pregnancy. O₂ saturations should be kept >92% to facilitate fetal oxygen delivery. Permissive hypercapnea may produce fetal acidemia with associated fetal heart rate changes. Airway pressure-release ventilation (ARPV) has been reported to be successful in management of Acute Respiratory Distress Syndrome (ARDS) in pregnancy. This mode starts at an elevated baseline pressure to facilitate oxygenation and lung recruitment and is followed by a deflation of pressure (release) to accomplish tidal volume ventilation and promote CO₂ removal. Spontaneous ventilation is allowed in this mode. This technique may lower airway pressures and have minimal circulatory effects with the added benefit of decreased sedation requirements.^{17,18,19,20} Blood gases will need to be drawn frequently to monitor oxygenation and arterial pH.

In severe ARDS cases that continue to decompensate despite traditional mechanical ventilation, extra-corporal membrane oxygenation (ECMO) has been successful. In a cohort of 12 patients (the largest published from H1N1 pandemic), 8 patients (66%) were successfully weaned from ECMO and all survived to hospital discharge. In addition, 5 (71%) patients delivered on ECMO and survived. Complications from ECMO included bleeding requiring transfusions (67%), nosocomial infection (58%), and preterm birth.²¹

Sedation and Medication

Most of the sedatives, anxiolytics, and narcotics commonly used in the ICU have potential side effects and are labeled categories C and D. However, their use is generally safe and can be justified when medically indicated in the parturient needing advanced management of mechanical ventilation. Benzodiazepines are category D drugs which cross the placenta. They

may increase the risk of preterm birth but do not seem to be associated with major congenital malformations when given early in pregnancy.^{22,23} When given close to delivery, they place the neonate at risk of respiratory depression, floppy infant syndrome, and potential withdrawal syndromes.^{24,25} Propofol is thought to produce sedation through activity at the γ -aminobutyric acid A (GABA_A) receptors but different from benzodiazepines. It readily crosses the placenta and fetal concentrations are roughly half of maternal concentrations within minutes. There is minimal placental metabolism. Two case reports exist of Propofol use as a continuous infusion for maintenance of anesthesia during neurosurgical cases prior to delivery. Both patients gave birth to healthy full term babies.^{26,27} It is a category B drug and appears to be safe when used short term. If given close to delivery, respiratory depression may occur in the neonate.

Dexmedetomidine is a selective α -agonist that produces stimulation of presynaptic α_2 receptors, resulting in presynaptic decreases in norepinephrine release and inhibition of postsynaptic activation. It provides sedation analgesia and anti-shivering properties without respiratory depression. Only limited data exist regarding the safety and efficacy of dexmedetomidine in pregnancy. It has limited effects on uteroplacental blood flow, and minimal placental transfer. It is a category D drug. The existing literature on its use in the parturient consists of case reports to help facilitate awake fiber-optic intubations, as an adjunctive analgesia for labor, during cesarean sections, and during emergence from anesthesia after a cesarean section in a patient with pulmonary hypertension.^{28,29,30} In vitro studies have shown that dexmedetomidine can augment spontaneous contractions in isolated human myometrium.³¹ Narcotics have a high lipid solubility and low molecular weight which easily allow them to cross the placenta. The neonatal metabolism is prolonged compared to adults. They can result in decreased beat to beat variability in fetal heart tracings. No congenital defects have been reported in association with any of the short term use of narcotics. However because of limited data they are classified as category D. When given close to delivery, narcotics can place newborns at risk of withdrawal and respiratory depression.^{1,18,32} Neuromuscular blocking agents minimally cross the placenta (because of their large molecular weight) and appear to be safe when given for short durations at time of cesarean section or as a single dose. Neonates tend to be more resistant to the neuromuscular blocking effects of these agents so that when normal doses are given to the mother, there is no discernable clinical effect on the fetus.³³ The neuromuscular blocking agents have been used safely in pregnant women ventilated for ARDS and help to decrease peak airway pressures when given with sedation.^{1,18} Magnesium sulfate can interact with neuromuscular blocking agents and tends to prolong duration of action.

United States Food and Drug Administration Pharmaceutical Drug Safety Categories During Pregnancy

Category A - Adequate and well controlled human studies failed to demonstrate a risk of fetal abnormalities

Category B - Animal studies have failed to demonstrate a risk to the fetus and there are no adequate and well controlled studies in pregnant women OR animal studies have shown an adverse effect, but adequate and well-controlled studies in humans have failed to demonstrate a risk to fetus

Category C - Animal studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant the use of the drug in pregnant women despite potential risk

Category D - Studies in pregnant women have demonstrated a risk to the fetus but potential benefits may warrant the use of the drug in pregnant women despite potential risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease or which safer drugs cannot be used or are ineffective)

Category X - Serious studies in animals or humans have demonstrated fetal abnormalities: use of the product is contraindicated in women who may be pregnant.¹

The known side effects of medications used in obstetrics may sometime have an adverse effect on critically ill patients. Beta agonist can cause tachycardia and decreased blood pressure. Indomethocin may have effects on platelet function and renal perfusion. Magnesium sulfate may have negative inotropic effects on cardiac function.¹²

Fetal Monitoring

Arrangements should be made to monitor the fetal heart rate tracings. Adverse changes in fetal heart tracing should encourage one to reassess blood pressure, hypoxemia, acidosis, or aortocaval compression. Correction of these factors may result in improvement of fetal heart tracings and are part of intrauterine resuscitation of the fetus. Fetal resuscitation in-utero through maternal oxygen therapy and circulatory support is preferable to cesarean delivery for non-reassuring fetal heart rate in most cases.^{1,12}

Decision to Deliver

There is conflicting data as to whether delivery of the fetus will improve the outcome in the pregnant patient with severe respiratory insufficiency. There is some indication that there can be clinical improvement in ventilatory settings and oxygen requirements after delivery in very severely compromised patients.^{34,35} Other studies have shown no real improvement after delivery.¹⁷

If vaginal delivery is done in the ICU, it is advantageous for anesthesia to be involved so that the mother can have an assisted second stage. Parenteral narcotics are less effective than regional anesthesia. When patients are ventilated and/sedated, positioning for regional may become a challenge. There may be hemodynamic changes with the institution of a neuraxial block, and the patient's coagulation status needs to be considered.

Cesarean section may allow for more rapid delivery but can be associated with a high amount of physiological stress which may have a higher mortality.¹⁸ In all case reports describing cesarean delivery, maternal hypoxemia or maternal decompensation was more frequently the indication for cesarean delivery than fetal considerations.³ Cesarean delivery can be done with an intravenous technique if the patient is already intubated, but the disadvantages of limited space for anesthesia, surgical, and neonatal equipment exist if done in the ICU. Also ICU's have a higher rate of nosocomial infections. Cesarean delivery in the ICU should be restricted to cases where the patient cannot be transported to the OR safely and expeditiously or for postmortem

procedures.¹²

When patients are transported to the operating room, care must be taken to maintain the patients' respiratory, and ventilation settings. PEEP valves need to be available. Occasionally, transport ventilators should be used to move patients. The decision to deliver must be individualized taking into account both maternal and fetal conditions.^{1,12,17}

References

1. Honiden, S, Abdel-Razeq S, Siegel MD,. The management of the Critically Ill Obstetric Patient. *J of Intensive Care Medicine*.2013;28(20):93:1-6
2. Siston AM, Rasmussen SA, Honein MA et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA* 2010;303:1517-1525
3. Mosby LG, Rasmussen SA, Jamieson DJ,. 2009 Pandemic influenza A (H1N1) in pregnancy a systemic review of the literature. *Am Journ of Ob & Gyn*. 2011; 25:10-18.
4. Louie JK, Acosta M, Jamieson DJ, Honein MA,. Severe 2009 H1N1 in pregnant and postpartum women in California. *N Eng J Med* 2010;362:27-34
5. Lapinsky SB,. H1N1 novel influenza A in pregnant and immunocompromised patients. *Crit Care Med* 2010;38(4) e52-e57
6. Ison MG. Clinical use of approved influenza antivirals: therapy and prophylaxis. *Influenza and Other Respiratory Viruses* 2012;7(Supp 1) 7-13
7. Brito V, Nierderman MS. Pneumonia Complicating Pregnancy. *Clin Chest Med*. 2011;32:121-132
8. Donner B, Niranjana V, Hoffmann G. Safety of oseltamivir in pregnancy: a review of clinical data. *Drug Saf* 2010;33(8):631-42
9. Lederman MM. Cell-mediated Immunity and Pregnancy. *Chest* 1984;86(3): Supp 6S-9S
10. Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Lai ST, Ho LC, A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *BJOG*. 2004;111:771-774
11. Dodds L, McNeil SA, Fell DB, Allen VM, Coombs A, Scott J, MacDonald N. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *CMAJ*. 2007;176(4):463-8
12. ACOG Practice Bulletin Number 100, Clinical Management Guidelines for Obstetrician-Gynecologist , Critical Care in Pregnancy. *Obstet Gynecol* 2009; 113(2):443-50
13. Sandrock C, Stollenwerk N,. Acute febrile respiratory illness in the ICU; reducing disease transmission. *Chest* 2008;133(5):1221-31
14. King TA, Adams AP. Failed intubation *Br J Anaesth*. 1990;65(30): 400-414.
15. Stamer UM, Messerschmidt A, Wulf H, Hoefl A. Equipment for the difficult airway in obstetric Units in Germany. *J Clin Anesth* 2000;12:151-156
16. Turkstra TP, Armstrong PM, Jones PM, Quach T,. GlideScope® use in the obstetric patient. *Int J Obstet Anesth* 2010. 19(1);123-4
17. Jahromi GS, Zand F, Khosravi A,. Acute respiratory distress syndrome associated with H1N1 influenza during pregnancy. *Int J Obster Anesth*. 2010;19(4):465-6
18. Jenkins TM, Troiano NH, Graves CR, Baird SM, Boehm FH,. Mechanical ventilation in an obstetric population: Characteristics and delivery rates. *Am J Obstet Gynecol*. 2003; 188:549-552
19. Hirani A, Marik PE, Plante LA,. Airway Pressure-Release Ventilation in Pregnant Patients

ANESTHESIOLOGY™ 2014

OCTOBER 11-15 | NEW ORLEANS, LA

- with Acute Respiratory Distress Syndrome: A Novel Strategy. *Resp Care* 2009. 54 (10): 1405-1408
20. Frawley PM, Habashi NM. Airway Pressure Release Ventilation: Theory and Practice. *AACN Clinical Issues* 2001;12(2); 234-246
21. Nair P, Davies AR, Beca J, Bellomo R, Ellwood D, Forrest P, Jackson A, Pye R, Seppelt I, Sullivan E, Webb S. Extracorporeal membrane oxygenation for severe ARDS in pregnant and postpartum women during the H1N1 pandemic. *Intensive Care Med* 2011; 37:648-654
22. Wikner BN, Stiller C, Bergman U, Asker C, Kallen B. Use of Benzodiazepines and benzodiazepine receptor agonists during pregnancy; neonatal outcome and congenital malformations. *Pharmacoepidemiology and Drug Safety* 2007;16:1203-1210
23. Bellantuono C, Tofani S, DiSciascio G, Santone G. Benzodiazepine exposure in pregnancy and risk of major malformations: a critical review. *General Hospital Psychiatry* 2013; 35:308
24. McElhatton PR. The effect of benzodiazepine use during pregnancy and lactation. *Reprod Toxicol.* 1994;8(6):461-75
25. Brigg GG, Freeman K, Yaffe SJ, Editors. *Drugs in pregnancy and Lactation. A reference guide to fetal and neonatal risk.* 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins: 2008
26. Tajchman, SK, Bruno JJ. Prolonged Propofol use in a critically ill pregnant patient. *Annals of Pharmacology.* 2010; 44: 2018-2022
27. Hilton G, Andrzejewski JC. Prolonged propofol infusions in pregnant neurosurgical patients. *J Neurosurg Anesthesiol* 2007;19:67-8
28. Neumann MM, Davio MB, Macknet MR, Applegate RL. Dexmedetomidine for awake fiberoptic intubation in a parturient with spinal muscular atrophy type III for cesarean delivery. *Int J of Obstet Anesth.* 2009;18(4):403-407
29. Palanisamy A, Klickovich RJ, Ramsay M, Ouyang DW, Tsen LC. Intravenous dexmedetomidine as an adjunct for labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord. *Int J Obstet Anesth* 2009;18(3):258-261
30. Toyama H, Wagatsuma T, Ejima Y, Matsubara M, Kurosawa S. Cesarean section and primary pulmonary hypertension: the role of intravenous dexmedetomidine. *Int J Obstet Anesth* 2009;18(3):262-267
31. Sia AT, Kwek K, Yeo GS. The in vitro effects of clonidine and dexmedetomidine on human myometrium. *Int J Obstet Anesth* 2005;14:104-7
32. Chestnut DH, Polley LS, Tsen LC, Wong CA, Chestnut's Obstetric Anesthesia Principles and Practice 4th Edition. 2009 Mosby Elsevier Philadelphia Pa. p 416-423
33. Booi LHDJ. Neuromuscular transmission and its pharmacological blockade. Part 4: Use of relaxants in paediatric and elderly patients, in obstetrics, and in the intensive care unit. *Pharm World Sci.* 1997;19(1):45-52
34. Daily WH, Katz AR, Tonnesen A, Allen SJ. Beneficial effect of delivery in a patient with adult respiratory distress syndrome. *Anesthesiology* 1990;72:383-6
35. Tomlinson MW, Caruthers TJ, Whitty JE, Gonik B. Does Delivery improve maternal condition in the Respiratory-Compromised Gravida? *Obstet Gynecol.* 1998;91:108-11