

## Impact of Intensive Care Management of Life Threatening Asthma on Feto-Maternal Outcome

Wafaa Ali Hassan<sup>1\*</sup>, Atef Darwish<sup>1</sup> and Zin A Zareh<sup>2</sup>

<sup>1</sup>Department of Chest Diseases, Obstetrics and Gynecology, Assiut and Women's Health University Hospitals, Assiut, Egypt

<sup>2</sup>Department of Anesthesia and Intensive care, Assiut and Women's Health University Hospitals, Assiut, Egypt

### Abstract

**Background:** The pregnant patient with medical complications represents a unique challenge to the intensive care specialist and often requires the management expertise of several subspecialists.

**Aim:** to evaluate the impact of intensive care management on the maternal and fetal outcomes in pregnant women with life threatening asthma.

**Patients and methods:** Twenty six obstetric patients with life threatening asthma admitted to the maternal intensive care unit (MICU) of Woman's Health Hospital during a 2-year Period from January 2010 through May 2012 were included in this study. Data collected included asthma history, ICU management, maternal and fetal outcome.

**Results:** All patients had history of persistent asthma (mild 27%, moderate 50%, severe 13%); most were receiving inhaled  $\beta$  agonist and corticosteroid preparations before the life threatening attack. Five only stopped taking any medications during pregnancy. Controlled mechanical ventilation was required in 5 patients (19%). The severity of hypercapnia ranged from 48 to 82 mm Hg. Two cases had preclampsia, 2 gestational diabetes, vaginal bleeding and premature rupture of membrane in one case and preterm birth in 2 cases. Twenty two cases were delivered by C.S (85%).

**Conclusions:** Obstetric patients with asthma are at risk for the development of life-threatening status asthmaticus, requiring MICU admission. The need for close interdisciplinary communication between obstetricians, intensivists and chest physicians to optimize maternal and fetal outcome is emphasized.

**Keywords:** Life threatening asthma; Intensive care unit; Pregnancy

### Introduction

The pregnant patient with medical complications represents a unique challenge to the intensive care specialist and often requires the management expertise of several subspecialists. The best place for proper management of these cases remains controversial. Although some tertiary care centers have maternal-fetal ICUs, many do not and use a general medical ICU to assist in the care of critically ill pregnant patients [1,2]. There is abundant literature on the management of asthma during pregnancy; however the literature is very limited in those with ASA who require Intensive care unit admission [3,4]. A life threatening episode indicates the presence of one of the three clinical types; acute severe asthma (an acute episode of bronchospasm where the FEV<sub>1</sub> is 30% or less than the predicted value), status asthmaticus (where the episode becomes resistant to  $\beta$ -adrenergic agonists and corticosteroids), or acute fulminant asthma (where the onset is rapid and severe and the patient is obtunded) [2]. Life threatening asthma in pregnancy poses difficult problems. In particular, the decision about when and where to deliver the fetus is complex, since maternal response to asthma treatment is unpredictable. Another problem is permissive hypercapnia, commonly practiced during life threatening asthma in the nonpregnant state, may not be safe during pregnancy as it affects uterine blood flow [5].

### Aim of the Work

This study was done in a maternal-fetal ICU of Woman's health Hospital, Assiut University, to ascertain a better understanding of the unique problems that pregnant patients with acute severe asthma present to the medical intensive care specialist.

### Patients and Methods

All obstetric patients with Acute Severe Asthma (ASA) admitted

to the intensive care unit of Woman's Health Hospital during the 2-year Period from January 2010 through May 2012 were included in this study. Data collected included asthma history, management plan in the Intensive Care Unit, ventilator management, maternal and fetal outcome.

The general, initial emergency department management for all patients admitted for ASA included: continuous nebulized salbutamol (until an adequate clinical response occurs) and intravenous hydrocortisone. The patient's speech, conscious state, pulse and respiratory rate, peak expiratory flow rate, oximetry and blood gases should be monitored, and if there is no improvement or the patient deteriorates, admission to an intensive care unit is required. In the MICU, invasive arterial monitoring was established and a urinary catheter inserted. Treatment with intravenous steroids (hydrocortisone 200 mg immediately then 100 mg four times a day), nebulized bronchodilators (salbutamol 5 mg 4-hourly and ipratropium bromide 500  $\mu$ g 4-hourly), an intravenous aminophylline infusion (2mg/kg, followed by 4 mg/kg over 30 minutes), high dose inhaled corticosteroids, intravenous magnesium sulphate (5-10 mmol as a bolus with 40 mmol over 1-2 hours) and supplemental humidified oxygen therapy to achieve oxygen saturations >92% [6]. Intravascular volume depletion was corrected

**\*Corresponding authors:** Wafaa Ali Hassan, Assistant Professor of chest diseases, Faculty of Medicine, Assiut University, 71111 Assiut, Egypt, Tel: 088-2340565; E-mail: [wafaagadallah@yahoo.com](mailto:wafaagadallah@yahoo.com)

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with normal saline. With further deterioration or for the management of acute fulminant asthma, endotracheal intubation with mechanical ventilation may be required. Volume assist-control mode of mechanical ventilation, low respiratory rate (8-10/ m), low tidal volume (6-8 ml/kg), high peak inspiratory were the strategies commonly used [7]. If hyperinflation and auto-PEEP were present, minute ventilation was reduced. Sedatives were required using propofol to facilitate controlled ventilation [8].

Fetal monitoring with an external cardiotocograph was done for all cases. In view of apparent fetal distress or worsening maternal asthma, a decision to deliver the fetus by caesarean section under general anaesthesia in a theatre, which is adjacent to the critical care unit. Anaesthesia was induced with alfentanil, midazolam and etomidate, and suxamethonium was used to facilitate intubation [9]. Anaesthesia was maintained with oxygen, air and sevoflurane, and muscle relaxation augmented with vecuronium [10]. Following delivery, a 5-unit bolus of oxytocin and an infusion of 40 units over 6 h were given i.v. and misoprostol 400 mg was given rectally to avoid uterine atony after  $\beta$ -agonist use Prostaglandin F<sub>2a</sub> was specifically avoided, due to its ability to induce bronchospasm [11]. Analgesia was maintained with a fentanyl infusion and rectal paracetamol 1g 6-hourly. Non-steroidal anti-inflammatory drugs were specifically avoided [12].

## Results

This study included 26 pregnant women with life threatening asthma. These 26 patients were in different stages of pregnancy. All patients had ASA asthma exacerbation not responding to the ED medications. Table 1 shows the patient characteristics. Four patients only had previous history of acute severe asthma attacks. All patients had persistent asthma (mild 27%, moderate 50%, severe 13%); most were receiving inhaled  $\beta$  agonist and corticosteroid preparations which were discontinued in 5 patients. Regarding maternal outcome, 3 cases had mild preeclampsia (11%), 2 cases had gestational diabetes (8%), vaginal bleeding and premature rupture of membrane in one case (4%), and preterm birth in 2 cases (8%). Twenty-two cases were delivered by C.S (85%) (Table 2). No fetal malformations, 2 cases of still birth (8%), 2 cases of twins (8%) and Low birth weight in 6 cases (24%). Controlled mechanical ventilation was required in 5 cases (19%). The severity of hypercapnia ranged from 48 to 82 mm Hg and duration of hypercapnia ranged from 50 minutes to 72 hours. All mechanically ventilated cases were delivered by CS (2, preterm, 3 fullterm).

## Discussion

The unique physiologic changes of pregnancy, impact of the fetus on the maternal condition, and concerns for fetal and maternal health and survival are particular concerns in management of bronchial asthma during pregnancy [1]. Furthermore, the issues of hypoxemia and hypercapnia, ventilator management and complications make this disease an especially important area for discussion. The literature concerning the effect of asthma on maternal and fetal outcome is conflicting and inconsistent [5]. Recent evidence supports that pregnant asthmatic women with moderate to severe asthma may have an increased risk of adverse perinatal outcomes [6]. The goal of asthma management during pregnancy is to optimize maternal and fetal health. Associations with asthma exacerbations include: low birth weight, preterm labor and delivery, preeclampsia, hyperemesis gravidarum, oligohydramnios, congenital malformations, gestational diabetes, increased risk of cesarean section, and perinatal mortality. These complications were thought to be related to recurrent hypoxia especially in poorly controlled asthma, medications used to treat

asthma, as well as demographic and socioeconomical factors associated with asthma. On the basis of the medical literature, there is consensus that good control of asthma is the most important determinant of maternal and perinatal outcomes [2,5].

We report our Maternal Intensive Care unit (MICU) experience in the management of ASA in 26 pregnant patients. The data concerning the safety of systemic corticosteroids during pregnancy are conflicting. Some studies showed no increase in birth defects in humans, others showed that their use especially during the first trimester is associated with a 3-fold increased risk for isolated cleft lip with or without cleft palate, as well as increasing risk of preterm delivery, low birth weight, and preeclampsia. However, due to the major benefit of systemic corticosteroids in severe asthma, the National Asthma Education and Prevention Program (NAEPP) recommends its usage during severe asthma exacerbation [13]. They are considered category C. Apgar<sup>™</sup> reported an increased incidence of cleft palate in two series of pregnancies in women treated with systemic corticosteroids in early pregnancy [14]. In this study, the incidence of still birth was 8%, and related to stoppage of treatment. No cleft palate or other malformations was reported. The incidence of stillbirths was eight times higher in women having continuous steroid treatment than in a corresponding group of untreated women with the same diseases [15]. The alarming findings in these studies may in part be the result of severe underlying disease rather than the treatment. Two studies of pregnant asthmatic women, some having short term and some long term systemic corticosteroids, showed no complications attributable to steroid treatment [16,17]. An association between asthma and preeclampsia of pregnancy has been reported and attributed to chronic steroid use [18,19]. We confirmed this association in our study (11%).

For pregnant patients with ASA requiring mechanical ventilation, there are several particular areas of concern: sedative administration to achieve controlled ventilation and the approach to mechanical ventilation. Sedation is crucial to achieve optimal ventilation. The safety of continuous sedative usage in pregnant patient is unknown [20].

Character	No (%)
Age ( $\pm$ SD)	26 $\pm$ 5.6
Gestational age (w)	32 $\pm$ 3
Asthma history	
Mild	13 (50%)
Moderate	6 (23%)
Severe	4 (15%)
Previous ASA attack	3 (11%)
Duration of MICU stay (d)	7 $\pm$ 3
Pharmacologic treatment	
Inhaled $\beta$ agonist	22 (85%)
Inhaled steroid	14 (54%)
Oral steroid	3 (11%)
Stopped treatment	5 (19%)
Blood gases	
PH	7.49 $\pm$ 02
PO <sub>2</sub>	85 $\pm$ 11
PCO <sub>2</sub>	22 $\pm$ 6

Table 1: Patient characteristics (26 cases).

Disorder	No (%)
Preeclampsia	3 (11%)
Gestational diabetes	2 (8%)
Maternal mortality	0
Bleeding during pregnancy	1 (4%)
Premature rupture of membrane	1(4%)
Preterm birth	2 (8%)

Table 2: Maternal outcome.

All of our 5 intubated obstetric patients were sedated with propofol. Propofol is a sedative-hypnotic with no analgesic action. Because of its short duration of action and bronchodilator effect propofol is the main sedative used for our asthma patients [20]. There is no clinical data to suggest that it is teratogenic [21]. No deleterious effect was found on oocytes in women undergoing assisted reproductive technology [22]. However it is very important to avoid hypotension, the most common side effect, because of the risk of decreasing uteroplacental blood flow, and not to exceed the recommended dose because it might lead to significant reduction in uterine smooth muscle tone [23]. In our MICU, we avoid benzodiazepine administration in intubated obstetric patients, particularly during the first trimester due to its teratogenic effect [24-26]. To our knowledge there is no data concerning the safety of opiates during short-term continuous sedation. The administration of therapeutic paralysis is generally avoided in patients with status asthmaticus in general because of concern of prolonged weakness and myopathy. It is considered pregnancy category B [27]. We did not need to use any neuromuscular blockade in any of our mechanically ventilated cases.

The degree of hypercapnia while patients were receiving controlled ventilation was striking and reflected the intense airways disease [28]. We have shown that these patients and their pregnancies could tolerate hypercapnia. The mortality rate of status asthmaticus has improved over recent decades. No mortalities were recorded in our study. One of the factors believed responsible for this reduction in mortality of ventilated patients is the acceptance of permissive hypercapnia and reduction of dynamic hyperinflation [29]. In general, a slow respiratory rate, low tidal volume, high peak inspiratory flow rate are set to allow greater time for exhalation of the tidal volume and therefore prevent air-trapping. Permissive hypercapnia has not been studied in pregnancy. Theoretically, maternal respiratory acidosis could lead to fetal acidosis, shift of the fetal hemoglobin dissociation curve to the right and consequently impaired oxygenation of fetal hemoglobin. An animal model suggested that maternal hypercapnia (PaCO<sub>2</sub> greater than 60 mm Hg) may lead to increased uterine vascular resistance and decreased uteroplacental blood flow [29]. In humans, there were no adverse effects of maternal hypercapnia induced for the period of labor [30]. In the published literature, they cited good pregnancy outcomes despite extreme hypercapnia [30-33]. In our series of 5 pregnant patients with status asthmaticus required intubation, they all had also good maternal outcome but their babies were low birth weight. Maternal hypoxia is well known risk that results in intrauterine growth retardation and death. Maintaining adequate maternal oxygenation during mechanical ventilation, PaO<sub>2</sub> in the range of 65 mm Hg is considered safe [31].

There are several small series of use of noninvasive ventilation in status asthmaticus [34,35]. Noninvasive ventilation has been used successfully in pregnant patients with obstructive sleep apnea and severe kyphoscoliosis [36]. In pregnant patients with status asthmaticus, NIV may support ventilation while the bronchodilators and corticosteroids are taking effect but gastric over-distention may be worsened.

In summary, this study highlights several important problems in managing pregnant women with acute severe asthma. Obstetric patients with asthma are at risk for the development of life-threatening status asthmaticus, requiring MICU admission. Permissive hypercapnia can be tolerated during pregnancy. The need for close interdisciplinary communication between obstetricians, Intensivist and chest physicians to optimize maternal and fetal outcome. This close collaboration should prevent most of the serious obstetric and neonatal complications of severe asthma during pregnancy (Table 3).

Disorder	No (%)
Malformation	0
Perinatal death	0
Still birth	2 (8%)
Twins	2 (8%)
Low birth weight	6 (24%)
Normal vaginal delivery	4 (15%)
Cesarean section	22 (85%)

**Table 3:** Neonatal outcome and methods of delivery.

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