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Asthma in Pregnancy

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Abstract: *Bronchial asthma is most common chronic condition in pregnancy complicating 4%–8% of pregnancies. This illness is becoming an increasing concern, as its prevalence has increased among all women over the past decade. Studies have shown that pregnant asthmatic women have an increased risk of adverse perinatal outcomes, whereas controlled asthma is associated with reduced risks. In approximately one- third of women asthma becomes worse, in another one-third becomes less severe and in the remaining one-third it remains unchanged during Pregnancy. A good history and clinical examination usually suffice to diagnose asthma in most patients. Pulmonary function tests like measurement of peak expiratory flow rate (PEFR) with help of a simple tool called peak flow meter can also aid in the diagnosis of asthma. PEFR is the easiest & most commonly performed test. The general principles of the management and treatment of asthma are the same in pregnant women as in non-pregnant women and in men. The general principles of the management and treatment of asthma are the same in pregnant women as in non-pregnant women and in men. The ultimate goal of asthma therapy during pregnancy is to maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother. Other goals include to achievement of minimal or no maternal symptoms day or night, minimal or no exacerbations, no limitations of activities, maintenance of normal or near-normal pulmonary function, minimal use of short-acting 2-agonists, and minimal or no adverse effects from medications.*

I. Introduction

Bronchial asthma is a chronic inflammatory disease of the airways that is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli. It is the most common chronic condition in pregnancy[1] complicating 4%–8% of pregnancies[2]. This illness is becoming an increasing concern, as its prevalence has increased among all women over the past decade.[3-4] Studies have shown that pregnant asthmatic women have an increased risk of adverse perinatal outcomes [5-6] whereas controlled asthma is associated with reduced risks[7].The severity of asthma often varies during pregnancy. In approximately one- third of women asthma becomes worse, in another one-third becomes less severe and in the remaining one-third it remains unchanged during Pregnancy.[8-10]

Pathophysiology

The hormonal, immunological and physiological changes of pregnancy affect the asthma symptoms. Values of FEV1 throughout pregnancy are not significantly different from the non pregnant condition, and similarly the ratio of FEV1/VC or peak flow in patients with asthma; this stability means that criteria for diagnosis and monitoring of asthma do not change. The physiological changes such as increases in free cortisol levels may protect against inflammatory triggers, increase in bronchodilator substance such as progesterone may improve airway responsiveness ,increase in bronchoconstring substance such as prostaglandin $F_2\alpha$ may promote airway constriction, and similarly decreased activity of Placental 11 β hydroxysteroid dehydrogenase type 2 is associated with an increase in placental cortisol concentration and low birth weight. The modification of cell mediated immunity may influence maternal response to infection and inflammation.

The Effect Of Asthma On Pregnancy

The poorly controlled asthma can have adverse effects on both mother & foetus which may lead to increased risk of perinatal mortality, preterm delivery, caesarean delivery, intrauterine growth retardation, stillbirth etc[11]. But recent studies contradict this generalisation, Indeed, the more recent data suggest that most women with asthma will have an uneventful pregnancy course. For women with well controlled asthma, pregnancy outcomes are similar to those of women without asthma [12-15] . Women with more severe or poorly controlled asthma are prone to adverse perinatal outcomes. The study showed statistically significant increases in gestational diabetes, small for gestational age newborns and caesarean delivery for women with moderate to severe asthma, even with optimal control.[16]. Need for oral steroids for control of asthma was independently predictive of delivery prior to 37 weeks and low birth Weight (less than 2500 g). Pulmonary function testing was also predictive of pregnancy outcomes: an FEV1 less than 80% of predicted values was associated with preterm delivery, pre-eclampsia, cesarean delivery and small for gestational age newborns.[16]

Effect Of Pregnancy On Asthma

Asthma improves during pregnancy in one-third of women, worsens in one-third of women, and remains unchanged in one-third of women .Large number of studies have demonstrated that severity of asthma pre conceptionally and during early pregnancy is predictive of the clinical course during the remainder of the pregnancy.[17-18] Asthma symptoms tend to correlate with rhinitis symptoms, and women with more significant symptoms during pregnancy experience more asthma exacerbations as well[19]. Women pregnant with female foetuses experience more severe asthma symptoms than women pregnant with male foetuses.[20-21]. It has been postulated that the surge in androgens at 12–16 weeks' gestation produced by male foetuses has a protective effect on maternal asthma.

Diagnosis Of Asthma

The diagnosis of asthma is based on History, physical examination and pulmonary function tests. The signs and symptoms of asthma differ from patient to patient, and their severity may also vary in any given patient at different times. The clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing cough & chest tightness[22]. Episodic symptoms after incidental allergen exposure, seasonal variability of symptoms and a positive family history of asthma and atopic disease are also helpful diagnostic guides.

The physical examination of respiratory system may be normal due to variable nature of asthma symptoms. The most usual abnormal physical finding is wheezing on auscultation. However, in some people with asthma wheezing may be absent or only detected when the person exhale forcibly, even in presence of significant airflow limitation.

A good history and clinical examination usually suffice to diagnose asthma in most patients. Pulmonary function tests like measurement of peak expiratory flow rate (PEFR) with help of a simple tool called peak flow meter can also aid in the diagnosis of asthma. PEFR is the easiest & most commonly performed test. It is the fastest rate at which air can move through the airways during a forced expiration starting with fully inflated lungs. The peak flow varies according to age, sex and height.. They should establish with their physician their personal best baseline peak flow measurement which is used to compare future value: PEFR in pregnancy: 380–550 l/min, Green zone: >80% of personal best, Yellow zone: 50–80%, Red zone: <50%. The spirometric evaluation of asthma in pregnant patients is similar to that of non-pregnant patients, as airway mechanics do not change significantly during pregnancy. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, and peak expiratory flow are stable to slightly increase in pregnancy[11-15]. As in non-pregnant patients, the diagnosis of asthma can be confirmed by demonstrating reversible airflow limitation before and after bronchodilator inhalation or before and after initiation of empiric treatment for asthma[17].

II. Management Of Asthma

General Principles

The general principles of the management and treatment of asthma are the same in pregnant women as in non-pregnant women and in men[23-24]. The ultimate goal of asthma therapy during pregnancy is to maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother. Other goals include to achievement of minimal or no maternal symptoms day or night, minimal or no exacerbations, no limitations of activities, maintenance of normal or near-normal pulmonary function, minimal use of short-acting 2-agonists, and minimal or no adverse effects from medications. As in other situations, the focus of asthma treatment must remain on control of symptoms and maintenance of normal lung function.[25]

A detailed history and physical examination should be performed to identify signs/symptoms of asthma during the initial encounter with the patient. Optimally, this assessment should occur prior to conception in order to establish a baseline [26]. Patients who have not had a baseline status established prior to pregnancy should have it established at their first obstetric visit.[27-28]A detailed history of disease status during prior pregnancies should be elicited because asthma symptoms experienced during prior pregnancies are generally predictive of symptoms experienced in subsequent pregnancies in any given patient.[29] Patients should be encouraged to take an active role in their disease management, paying close attention to factors which affect their disease status and the onset of exacerbations[30]. Management or co-management of these patients by a physician with sufficient experience in caring for pregnant asthmatics improves outcome

Management of bronchial asthma during pregnancy can be divided in to four basic component of therapy.

1. Assessment and monitoring of asthma
2. Patients Education
3. Avoidance of triggers
4. Pharmacotherapy

Assessment &Monitoring:

Normal lung function is important to a mother's health and to her baby's well-being. Objective assessments and monitoring should be performed on a monthly basis. Such assessments should include pulmonary function testing (ideally spirometry), detailed symptom history (symptom frequency, nocturnal asthma, interference with activities, exacerbations, and medication use), and physical examination with specific attention paid to auscultation of the lungs. Schatz and colleagues[31] observed that 30% of subjects whose asthma was classified as mild at entry ''switched'' categories during pregnancy to the moderate or severe groups. Thus, pregnant asthmatic patients, even those who have mild or well-controlled disease, need to be monitored closely during pregnancy.

The FEV 1 after a maximal inspiration is the single best measure of pulmonary function. When adjusted for confounders, a mean FEV1less than 80% predicted has been found to be significantly associated with increased preterm delivery less than 32 weeks and less than 37 weeks, and birth weight less than 2,500 g.[32] However, measurement of FEV1 requires a spirometer. The PEFR correlates well with the FEV1, and has the advantages that it can be measured reliably with inexpensive, disposable, portable peak flow meters. Patient self-monitoring of PEFR provides valuable insight to the course of asthma throughout the day, assesses circadian variation in pulmonary function, and helps detect early signs of deterioration so that timely therapy can be instituted. Patients with persistent asthma should be evaluated at least monthly and those with moderate to severe asthma should have daily PEFR monitoring.[33]The typical PEFR in pregnancy should be 380–550 L/min. Patients should establish her "personal best" PEFR, then calculate her individualized PEFR zones: Green Zone more than 80% of personal best, Yellow Zone 50 to 80% of personal best, and Red Zone less than 50% of personal best PEFR.

A baby's well-being is monitored in a variety of ways during regular medical visits throughout pregnancy. These visits are particularly important for women who have asthma. Women should be aware of their baby's movements. If your baby is not moving normally, contact your obstetrical provider immediately. This is especially true for women who are also having asthma symptoms or an asthma attack. Non-stress testing is sometimes recommended after 32 weeks of pregnancy for women who have frequent asthma symptoms or attacks. The test is performed to assess the baby's condition. It is done by monitoring the baby's heart rate with a small ultrasound device that is placed on the mother's abdomen. The baby's heart rate should increase when it moves. The test is considered reassuring if two or more fetal heart rate increases are seen within a 20 minute period. Further testing may be needed if these increases are not observed after monitoring for 40 minutes. Ultrasound examination to check the baby's growth and activity, and also the amount of amniotic fluid around the baby, is sometimes performed

Education:

Pregnancy is a good time to review the patient's basic understanding of asthma and its management, including trigger avoidance, asthma control, and adequate use of devices, medication, and personal action plans. The patient must understand the potential adverse effects of uncontrolled asthma on the well-being of the fetus, and that treating asthma with medications is safer than increased asthma symptoms that may lead to maternal and fetal hypoxia. The patients should be able to recognize symptoms of worsening asthma and be able to treat them appropriately. All this requires an individualized action plan that is based on a joint agreement between the patient and the clinician. Correct inhaler technique should be assured, and the patient also should understand how she can reduce her exposure to, or control those, factors that exacerbate her asthma. Useful information is available on the websites of national Pulmonary societies and international organisations, and patients can be referred to these if they seek additional information.(Global Initiative for Asthma www.ginasthma.com)

Avoidance Of Triggers:

Avoidance of asthma triggers, such as animal dander, tobacco smoke, and Pollutants, is important because exposure may lead to increased asthma symptoms and the potential need for more medication. Often, allergen immunotherapy is effective for those patients in whom symptoms persist, despite optimal environmental control and proper drug therapy. Allergen immunotherapy can becontinued carefully during pregnancy in patients who are deriving benefit, who are not experiencing systemic reactions, and who are receiving maintenance doses. Benefit–risk considerations do not generally favor beginning immunotherapy during pregnancy for most patients because of (1) the undefined propensity for systemic reactions, (2) the increased likelihood of systemic reactions during initiation of immunotherapy, (3) the latency of immunotherapy effect, and (4) the frequent difficulty in predicting which asthmatic patients will benefit from im-munotherapy.[34] Smoking should be completely prohibited. Morbidity during pregnancy that is due to smoking may be independent of, and additive to, morbidity that is due to asthma[35].

Pharmacological Treatment:

Almost all antiasthma drugs are safe to use in pregnancy and during breastfeeding. In fact, under treatment of the pregnant patient is a frequent occurrence, because such patients are worried about medication effects on the fetus. Appropriate monitored use of theophylline, Inhaled glucocrticosteroids, β2 agonists and leukotriene modifiers (specially montelukast) is not associated with increased incidence of fetal abnormality.

Table 1. FDA Categories of Anti- asthma drug during pregnancy

Drug		Categories
Beta 2 agonist	Salbutamol	C
	Levosalbutamol	C
	Formoterol	C
	Salmeterol	C
Inhaled Coeticosteroid	Budesonide	B
	Beclomethasone	C
	Fluticasone	C
	Ciclesonide	C
	Mometasone	C
Leukotriene receptor antagonist	Montelukast	B
	Zafirlukast	B
Cromolyn		B
Theophylline		C

Drug for asthma categorise in two groups 1.Controller medication e. g Inhaled glucocorticosteroids, Leukotriene modifiers, Long-acting inhaled β_2-agonists in combination with inhaled glucocorticosteroids, Systemic glucocorticosteroids,Theophylline ,Cromones , Anti-IgE. 2. Reliever medication e.g. SABA (short acting beta-agonist), SAMA (Short acting Anticholinergic such as Ipratropium bromide).

Treatment Of Asthma During Pregnancy

Each patient should be assessed to establish his or her current treatment regimen, adherence to the current regimen and level of asthma control (Table 2). This working scheme have been developed and are validated for various application, including use by health care provider to assess the state of control of their patients asthma and patients for self assessment as part of a written action plan. Uncontrolled asthma may progress to exacerbation. B. Assessment of future risk such as risk of exacerbation, rapid decline in lung function, side effect. These factors are poor clinical control, frequent exacerbation in past year, ever admission to critical care for asthma, low FEV1, exposure to cigarette smoke.

Table 2. Level Of Asthma Control:

A. Asthma symptoms control	**Level of asthma symptom control**		
In the past 4 weeks, has the patient had:	Well Controlled	Partly controlled	Uncontrolled
Daytime asthma symptoms more than twice/weeks? Yes/No	None	1-2 of these	3-4 of these
Any night waking due to asthma? Yes/No			
Any activity limitation due to asthma Yes/No			
Reliever needed for symptoms more than twice/weeks? Yes/No			
B. Risk factors for poor asthma outcomes	Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbation. Need to measure FEV1 at start of treatment, after 3 month of controller treatment to record the patients personal best lung function, then periodically for ongoing risk assessment.		

Stepwise approach to pharmacologic therapy:

The patient's current level of asthma control and current treatment determine the selection of pharmacologic treatment. For example if asthma is not controlled on the current treatment regimen, treatment should be stepped up until controlled is achieved. If control has been maintained for at least three months, treatment can be stepped down with the aim of establishing the lowest step and dose of treatment that maintain control, if asthma is partly controlled, an increase in treatment should be considered, subject to whether more effective options are available (increase dose or an additional treatment), safety and cost of possible treatment and the patients satisfaction with level of control achieved. (Figure 1)

Figure 1. Stepwise approach in management of bronchial asthma in pregnancy

Management Approach Based On Control

Level of control	Reduce	Treatment action
Controlled		Maintain and find lowest controlling step
Partly controlled	Increase	Consider stepping up to gain control
Uncontrolled		Step up until controlled
Exacerbation		Treat as exacerbation

Decrease ← Treatment steps → Increase

Step 1	Step 2	Step 3	step 4	Step 5
Asthma education, Environmental control If step-up reatment considered for poor symptom control, check inhaler technique, adherence & confirms symptoms due to asthma				
SABA as on need basis	SABA as on need basis			
Controller option	Select one	Select one	Select one or more	To step four, add either
	Low dose ICS	Low dose ICS plus LABA	Medium or high dose ICS plus LABA	Oral Glucocorticoides (lowest dose)
	Leukotriene modifier	Medium or high dose ICS or Low dose ICS plus Leukotriene modifier	Leukotriene modifier	Anti-IgE treatment
		Low dose ICS plus sustained release theophylline	sustained release theophylline	

Key Features Of Asthma Treatment:

1. The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs
2. Each patient should be assessed to establish his or her current treatment regimen, adherence
3. to the current regimen and level of asthma control
4. Minimize use of short-acting inhaled beta2-agonist
5. At each treatment step, a reliever medication (rapid onset bronchodilator, either short acting or long acting) should be provided for quick relief of symptoms
6. Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens, irritants)
7. Refer to an asthma specialist if there are difficulties controlling asthma or if Step 4 care is required. Referral may be considered if Step 3 care is required.

Management Of Asthma During Exacerbation: Exacerbation of asthma are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness or some combination of these symptoms .An asthma exacerbation that causes minimal problem for mother may have severe sequelae for the foetus. A decrease in foetal movement may be an early manifestation of an asthma exacerbation Indeed abnormal fetal heart rate tracing may the initial manifestation of an asthmatic exacerbation. A maternal Po2 less than 60 or Hb saturation less than 90% may be associated with profound foetal hypoxia. Therefore, asthma exacerbation during pregnancy should be managed aggressively. Exacerbations are most likely to occur between 24 to 36 weeks of pregnancy.. Hence the most important part of managing such condition is prevention of exacerbation. The mechanisms that lead to asthma exacerbations during pregnancy are poorly understood, but viral infections and discontinuation of anti-inflammatory medications are likely to be important.[36-37]. Exacerbation are characterised by decreases in expiratory airflow that can be quantified by measurement of Lung function (PEF or FEV1). Effective management of exacerbations incorporates the same four components of asthma management used in managing asthma long term: assessment and monitoring, patient education, avoidance of triggers, and medications. Management depend upon severity of exacerbation.(Table 3) Asthma with mild to moderate exacerbation can be manage at the level of home but all severe exacerbation and some cases of moderate exacerbation should be manage in Emergency.

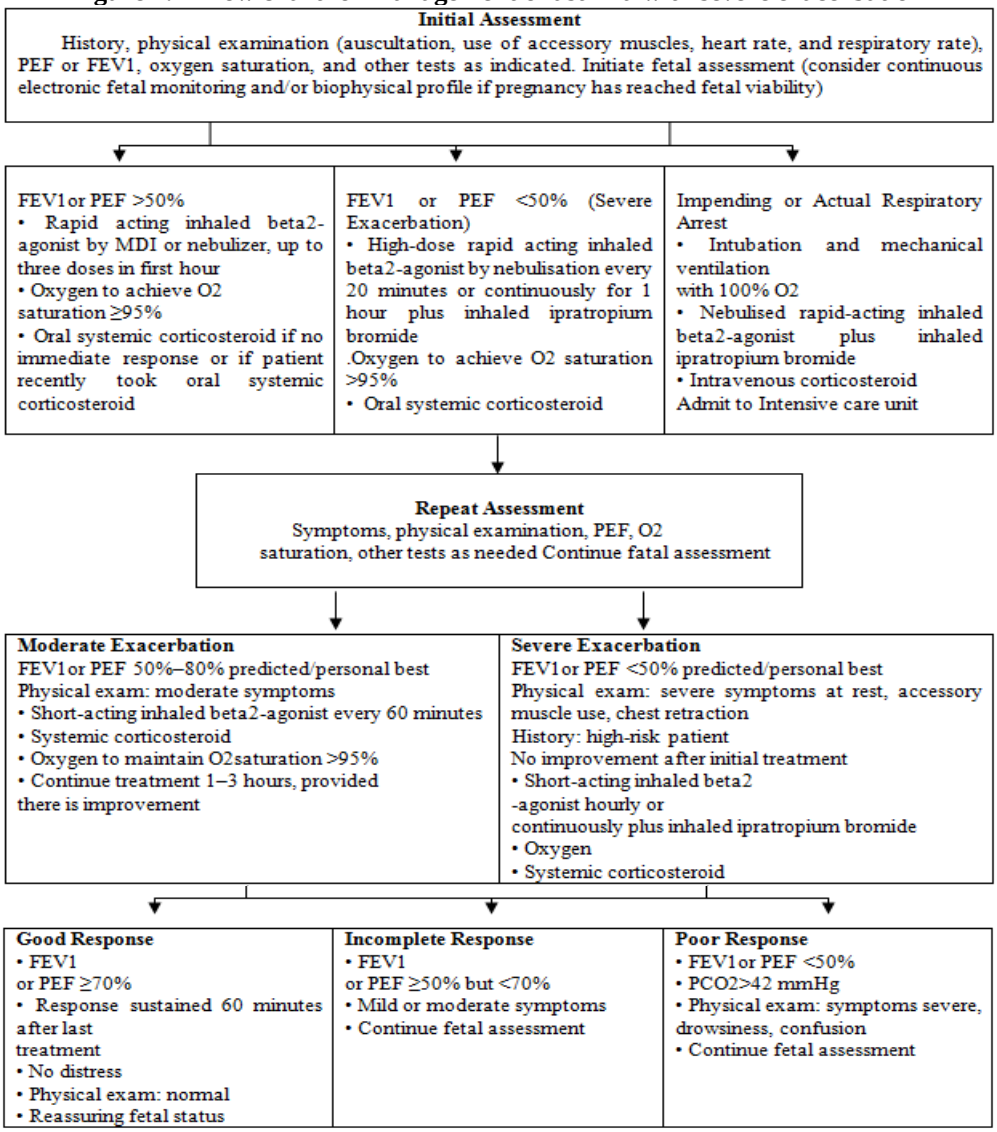
Table 3. Severity of asthma exacerbation

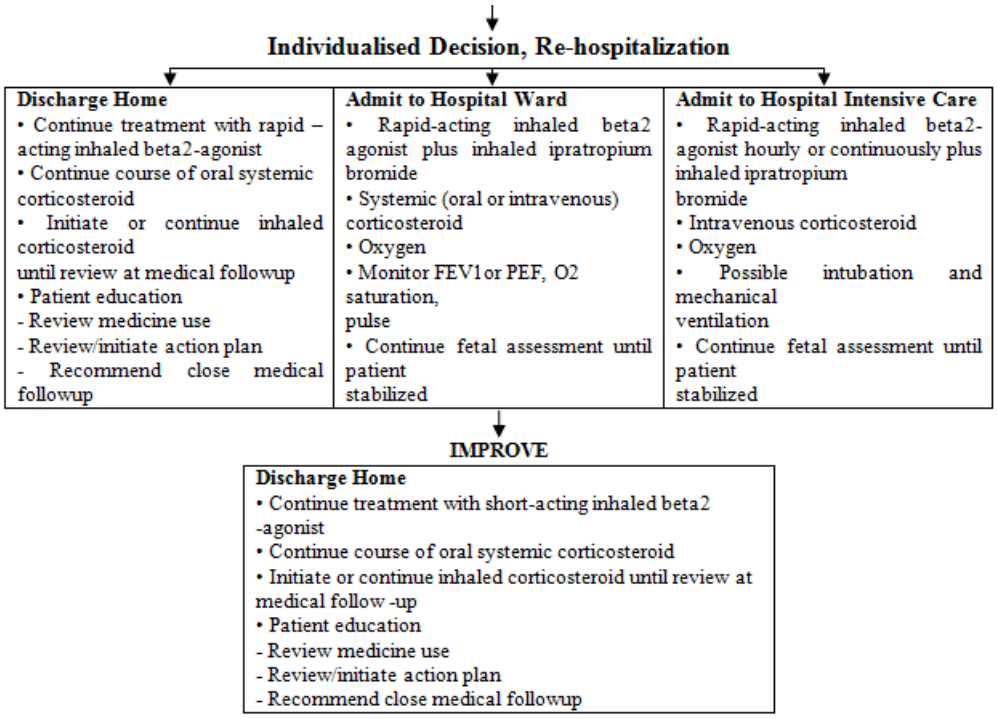
Severity	Symptoms & sign	PFT	Treatment
mild	Dyspnea only with activity	PEF over 80%	Home management
moderate	Dyspnea interferes with or limits usual activities	PEF 60-80%	Home management
severe	Dyspnea at rest, interfere with conversation	PEF <60% predicted	Require Hospitalisation
Very severe (Life threatening)	To dyspneic to speak, perspiring		ICU management

Home Management For Asthma Exacerbation: Patients should be given an individualized guide for decision-making and rescue management, and educated to recognize signs and symptoms of early asthma exacerbations such as coughing, chest tightness, dyspnea, or wheezing, or by a 20% decrease in their PEFR. This is important so that prompt home rescue treatment may be instituted to avoid maternal and fetal hypoxia. For mild to moderate exacerbation, repeated administration of rapid acting inhaled β2 agonist (2 to 4 puffs every 20 minutes for 1st hour) is usually best & most cost effective approach for reversal of airflow obstruction. If there is poor response defined by PEFR less than 50% predicted, or severe wheezing and shortness of breath, or decreased fetal movement, repeat inhaled β2 agonist 2–4 puffs by MDI and obtain emergency care. If there is incomplete response, PEFR is 50–80% predicted or if persistent wheezing and shortness of breath, then repeat inhaled β2 agonist treatment 2–4 puffs MDI at 20-minute intervals up to two more times. If repeat PEFR shows 50–80% predicted or if decreased fetal movement, contact doctor or go for emergency care .If there is good response PEFR more than 80% predicted, no wheezing or shortness of breath, and fetus is moving normally. May continue inhaled β2 agonist 2–4 puffs MDI every 3–4 hours as needed.

Hospital & Emergency Management: The principal goal should be the prevention of hypoxia. Measurement of oxygenation by pulse oximetry is essential, arterial blood gases should be obtained if oxygen saturation remains less than 95 percentage. Continuous electronic fetal monitoring should be initiated if gestation has advanced to point of potential fetal viability. To achieve arterial oxygen saturation of 90 percentages, oxygen should be administered by nasal cannulae, or by mask. Rapid acting inhaled beta2-agonist should be administered at regular interval. The most cost effective and efficient delivery by metered dose inhaler and spacer but occasionally nebulisation used (Figure 2).

Figure 2. Flow chart for management of asthma with severe exacerbation





FEV1: Forced expiratory volume in 1 second
MDI: Metered-dose inhaler
PCO2: Carbon dioxide partial pressure;
PEF: Peak expiratory flow

Management Of Asthma During Labor

Asthma exacerbation occurs in approximately 10-20% during Labor and delivery[38]. Asthma medications should not be discontinued during labor and delivery. If systemic corticosteroids have been used in the previous four weeks, then intravenous corticosteroids (eg, hydrocortisone 100 mg every 8 hours) should be administered during labor and for the 24-hour period after delivery to prevent adrenal crisis[39]. Asthma is usually quiescent during labor, consideration should be given to assessing PEFRs upon admission and at 12-hour intervals. The patient should be kept hydrated and should receive adequate analgesia to decrease the risk of bronchospasm. It is rarely necessary to perform a caesarean delivery for an acute asthma exacerbation. Usually, maternal and fetal compromise will respond to aggressive medical management. Occasionally, delivery may improve the respiratory status of a patient with unstable asthma who has a mature fetus. Prostaglandin E2 or E1 can be used for cervical ripening, the management of spontaneous or induced abortions, or postpartum haemorrhage, although the patient's respiratory status should be monitored[40]. Prostaglandin F2alpha and methylergonovine, which are used for postpartum hemorrhage, can induce bronchospasm[41]. Magnesium sulfate is a bronchodilator, but indomethacin can induce bronchospasm in the aspirin-sensitive patient. There are no reports of the use of calcium channel blockers for tocolysis among patients with asthma, although an association with bronchospasm has not been observed with wide clinical use. Lumbar anesthesia has the benefit of reducing oxygen consumption and minute ventilation during labor[42]. Fentanyl may be a better analgesic than meperidine, which causes histamine release, but meperidine is rarely associated with the onset of bronchospasm during labor. A 2% incidence of bronchospasm has been reported with regional anesthesia[43].) Ketamine is useful for induction of general anesthesia because it can prevent bronchospasm.

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