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Key points

- Asthma is the most common chronic disease to affect pregnant women.
- Exacerbations occur in up to 45% of pregnant women with asthma.
- Asthma should be managed during pregnancy as for other adults.
- Treatment adjustment using a marker of airway inflammation reduces the exacerbation rate in pregnancy.

Educational aims

- To identify the goals of and steps associated with effective asthma management in pregnancy.
- To understand the maternal and perinatal risks associated with asthma during pregnancy.
- To describe a management strategy that has been shown to reduce exacerbations in pregnant women with asthma.



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Managing asthma in pregnancy

Asthma is a common comorbidity during pregnancy and its prevalence is increasing in the community. Exacerbations are a major clinical problem during pregnancy with up to 45% of women needing to seek medical help, resulting in poor outcomes for mothers and their babies, including low birth weight and preterm delivery. The goals of effective asthma management in pregnancy are to maintain the best possible asthma control and prevent exacerbations. This is achieved by aiming to prevent day- and night-time symptoms, and maintain lung function and normal activity. In addition, maintaining fetal oxygenation is an important consideration in pregnancy. Guidelines recommend providing asthma advice and review prior to conception, and managing asthma actively during pregnancy, with regular 4-weekly review, provision of a written action plan, use of preventer medications as indicated for other adults with asthma, and management of comorbid conditions such as rhinitis.

Improvements have been made in recent years in emergency department management of asthma in pregnancy, and multidisciplinary approaches are being proposed to optimise both asthma outcomes and perinatal outcomes. One strategy that has demonstrated success in reducing exacerbations in pregnancy is treatment adjustment using a marker of eosinophilic lung inflammation, the exhaled nitric oxide fraction (F_{eNO}). The use of an algorithm that adjusted inhaled corticosteroids (ICS) according to F_{eNO} and added long-acting β -agonists when symptoms remained uncontrolled resulted in fewer exacerbations, more women on ICS but at lower mean doses, and improved infant respiratory health at 12 months of age. Further evidence is needed to determine whether this strategy can also improve perinatal outcomes and be successfully translated into clinical practice.



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Guidelines for the management of asthma during pregnancy exist but are too rarely used in clinical practice <http://ow.ly/U8Sq8>

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Introduction

Asthma is the most common chronic medical condition to be reported during pregnancy and its prevalence in the population has increased in recent decades. Kwon *et al.* [1] reported an increase in the prevalence of asthma during pregnancy from 3.7% in 1997 to 8.4% in 2001. More recent reports from the USA found a prevalence

of 5.5% in 2001, increasing to 7.8% in 2007 [2]. A prevalence of 9.3% has been reported in Ireland [3] and 12.7% in Australia [4]. Maternal asthma is associated with an increased risk of adverse perinatal outcomes, and changes in the course of the disease are to be expected and can be unpredictable during pregnancy. Optimising asthma management in pregnancy is paramount for protecting the health of both mother and baby.

Guidelines for the management of asthma during pregnancy

International guidelines are available that outline the goals of successful asthma management and recommendations for clinical management of asthma in pregnancy [5]. Goals include the prevention of chronic day and night symptoms, maintenance of optimal pulmonary function and normal activities, and prevention of exacerbations, using therapies with minimal or no adverse side-effects [5]. During pregnancy, there is the additional goal to maintain fetal oxygenation by preventing episodes of maternal hypoxia [5]. Achieving this requires regular monitoring of clinical symptoms, provision of self-management education and the correct use of pharmacotherapies. Multidisciplinary management by all health professionals involved in a woman's care is encouraged [5].

A stepwise approach to asthma treatment is recommended during pregnancy as for other adults with asthma [5]. Guidelines recommend the use of short acting β -agonists (SABA) as reliever medication and the use of inhaled corticosteroids (ICS) for women with persistent asthma [5]. There is much reassuring data concerning the safety of ICS medication use in pregnancy, particularly for budesonide, which has the best safety rating during pregnancy. Guidelines recommend the continued use of ICS medication that has been effective in controlling asthma prior to pregnancy [5].

In 2014, the Australian National Asthma Council released updated guidelines for asthma management (www.astmahandbook.org.au), including a section on pregnancy. These guidelines recommend managing asthma actively during pregnancy, as for asthma in other adults, including prescribing preventers if indicated, and stepping up the regimen as necessary with the goal to maintain the best possible asthma control and avoid exacerbations. Regular review of asthma every 4 weeks during pregnancy is recommended, with asthma control assessed each time. In addition, comorbidities such as rhinitis or gastro-oesophageal reflux, which can contribute to worsening asthma, should be identified and managed. In terms of exacerbations, the Australian guidelines recommend intervening early, providing a written action plan with a low threshold for seeking medical help and ensuring prompt treatment in emergency departments to minimise risks to the fetus. Preconception care is also suggested, with recommendations to offer advice that uncontrolled asthma or asthma exacerbations put both mothers and babies at risk, provide an asthma review prior to conception including performing baseline spirometry, offering a written action plan, smoking cessation advice and vaccinations as required, and discussing the

need to continue taking preventer therapies (if prescribed) when pregnant.

Despite clear guidelines for the management of asthma during pregnancy, there is evidence of suboptimal management in primary care. An Australian survey of 174 general practitioners (GPs) found that there was a lack of knowledge and confidence in managing asthma during pregnancy, with 25.8% of respondents indicating that they would stop or decrease ICS doses even among pregnant women whose asthma was well controlled on current therapy [6]. 12% of GPs indicated that they did not know how to manage a deterioration of asthma during pregnancy and would refer the patient to another health professional, while 67% would increase her dose. Although ICS were perceived to be the safest and preferred preventer medication for use in the first trimester, there was considerable concern about the safety of leukotriene receptor antagonists (LTRA) in the first trimester, with 45% of GPs indicating that they did not consider them safe, while many GPs did not consider long acting β -agonists (LABA) or oral corticosteroids (OCS) to be safe in the first trimester [6]. Nearly half of the respondents reported having patients who were non-adherent during pregnancy; however, 82% were likely to reinforce the need for continuing preventer medication among women who reported stopping this when becoming pregnant [6], which was an encouraging finding.

In Spain, a multiple-choice survey related to the use of asthma management guidelines for pregnant patients was completed in 2009 by 1000 healthcare professionals, including primary care physicians (46%), respiratory specialists (20%), allergy specialists (17%) and obstetricians (17%) [7]. While 96.5% of respondents indicated that they found guidelines useful, 64% also indicated that they seldom or never followed guidelines. Asthma in pregnancy guidelines were more likely to be used by respiratory and allergy specialists (56.6% and 60.4% respectively) than by primary care physicians (25.3%) or obstetricians (16.3%). Just over half of physicians would maintain asthma therapy in patients who were clinically stable, while 25.5% would suggest medications be used "on demand", 17.6% would send the patient to a specialist (47.7% of obstetricians answered this way) and 1% would withdraw all medication. 30% believed spirometry was not recommended in pregnant asthmatic patients, while 10% would use spirometry monthly and 37% only if symptomatic. Most allergists (83.7%) would continue with specific immunotherapy in pregnancy, while less than one-third of the other physicians would continue immunotherapy [7]. These data indicate a difference in the way asthma is managed in pregnancy depending on the healthcare specialist and reinforces the need for education for all of the multidisciplinary team managing a pregnant woman's asthma.

Use of asthma medications in pregnancy

Recently published data indicates that undertreatment of asthma during pregnancy remains an issue. Among women reporting having asthma, asthma medications were used by 63% in an American study (2001–2007) [2] and 62.9% in an Irish study (2000–2007) [3]. In the American study, around a quarter of these women were using ICS and a further 4% an ICS/LABA combination [2]. In the Irish study, 23% were using ICS [3]. A Korean study analysing data from 2009 to 2013 found that ICS was used by 15% of pregnant women with asthma, and ICS/LABA by a further 10.5% [8]. In a 2009 Australian survey, 19% of women were using a preventer for asthma treatment in pregnancy, while 57% of women reported use of reliever medication only and 24.5% of women were not using any pharmacological treatments [4]. This study also reported pre-pregnancy medication use and found that this period was associated with greater use of medications, with only 7.8% of women not using medication for asthma prior to pregnancy [4]. These data demonstrate a disconnect between asthma medication use prior to pregnancy and once pregnant, potentially due to changes in prescribing habits, perceived risks held by women or health professionals, or a change in asthma disease severity or control with pregnancy.

Nonadherence to prescribed ICS medications has been outlined in many studies of pregnant women with asthma [9]. A small study of 32 Turkish pregnant women with asthma was recently published [10]. More than half of the women (56%) were “irregular” users of asthma medication during pregnancy, which was not significantly different from pre-pregnancy (68%). During pregnancy, 52% of women were using ICS, while 22% did not use any medication for their asthma while pregnant. Exacerbations among this study population were high, with 13% hospitalised, 22% receiving OCS and 47% having an emergency visit during pregnancy [10], and undertreatment was likely a contributing factor. Pregnant women themselves perceive there to be a risk of using asthma medications during pregnancy. POWELL *et al.* [11] found that women assigned minimal risk to SABA such as salbutamol (0.5 cm on a 10-cm visual analogue scale), with greater risks for ICS (1.2 cm) and OCS (4.5 cm). This translates to a decline in asthma medication use, particularly in early pregnancy, with one study of prescriptions reporting a 13% decline in SABA use, a 23% decline in ICS use and 54% decline in OCS use in the first trimester compared to the 20 weeks prior to pregnancy [12].

Data has recently been published from the Xolair Pregnancy Registry, a prospective study of outcomes among 160 infants whose mothers used the anti-IgE medication omalizumab during

pregnancy [13]. Omalizumab is used in patients with moderate–severe asthma who are not adequately controlled with ICS. The majority of women monitored in this study were exposed to omalizumab during the first trimester, with a median total duration of exposure during pregnancy of 8.8 months. Infants were born at a mean gestational age of 38.3 weeks and among singletons, the rates of prematurity (14.5%), small for gestational age (10.9%) and low birth weight (3.2%) were consistent with data from other studies of women with asthma. Congenital malformations were reported in 20 infants, of which seven were considered major malformations. This registry is ongoing and further data are expected to be reported once 250 women have been recruited [13].

Asthma exacerbations and healthcare utilisation during pregnancy

Asthma exacerbations are a significant clinical problem during pregnancy. Up to 45% of pregnant women with asthma have moderate–severe exacerbations requiring medical intervention during pregnancy [14]. In addition to the adverse effect on maternal health, exacerbations are a key contributor to adverse perinatal outcomes in asthma. Exacerbations, oral steroid use and severe asthma are associated with preterm delivery, possibly due to maternal hypoxia, the effects of maternal inflammation and/or changes in uterine smooth muscle function [15]. In addition, women with exacerbations of asthma are three times more likely to have a low birth weight baby compared to asthmatic women without exacerbations [16], suggesting that prevention of exacerbations during pregnancy may also lead to improvements in perinatal outcomes.

In a Korean study of asthma during pregnancy, KIM *et al.* [8] found that the rate of hospitalisation for asthma was higher among pregnant women (1.3%) than nonpregnant women (0.8%), after adjusting for age and exacerbation history; however, the length of hospital stay and number of hospitalisations per person was no different between these groups. Emergency department treatment for asthma occurred in 0.4% of pregnant women with asthma, while the number of outpatient visits was significantly lower than for their nonpregnant counterparts, with an increase observed after delivery. In addition, the use of medications was significantly lower in pregnancy for ICS/LABA combinations, LTRA, SABA, systemic steroids, xanthine derivatives and systemic LABA. Asthma exacerbations (measured by hospital admission) were 2.7 times more frequent in the subgroup of women with newly diagnosed asthma during pregnancy, and outpatient visits and prescriptions for asthma medications were also more

frequent. Almost half of all women with newly diagnosed asthma were prescribed ICS or ICS/LABA combinations while only 14.6% of women with previously diagnosed asthma used these medications. However, the rate of hospitalisation and emergency department visits did not differ between these two groups. Overall, the proportion of women with hospitalisations (where OCS was prescribed for at least 3 days) increased from 0.2% in the first trimester to 0.5% in the second trimester and 0.7% in the third trimester. Severe exacerbations were experienced by 5.3% of participants [8], consistent with previous findings [17].

These studies demonstrate the potential for asthma status to markedly change during pregnancy and from trimester to trimester. Typically, approximately at least one-third of women with asthma report a worsening in their usual symptoms, one-third have no change and one-third have an improvement [18]. It is also recognised that women with mild disease are still at risk of severe exacerbations during pregnancy, and for this reason, regular monitoring of asthma during pregnancy is recommended [5].

Emergency department management of asthma exacerbations during pregnancy

Pregnant women with asthma exacerbations should be treated in the same way as nonpregnant adults with exacerbations. However, there is evidence from studies in emergency departments that this does not occur. A retrospective study from the USA compared OCS treatment during exacerbations among 123 pregnant and 123 nonpregnant women with asthma between 1996 and 2009 [19]. During the acute care visit, significantly more nonpregnant women were treated with OCS (72.4%) compared with pregnant women (50.8%), while 69% of nonpregnant women were prescribed OCS at discharge compared with 41% of pregnant women. The pregnant women were significantly more likely to return to the emergency department within 2 weeks of discharge (9.7%) compared with the nonpregnant women (2.5%) [19]. These data were comparable to an earlier multicentre study from 36 emergency departments in the USA, where 51 pregnant women were compared with 500 nonpregnant women with similar peak expiratory flow rates and duration of asthma symptoms [20]. Here, 66% of nonpregnant women were treated with OCS, compared with only 44% of pregnant women. In addition, the pregnant women were 2.9 times more likely to report an ongoing exacerbation at the 2-week follow-up compared with the nonpregnant women [20]. A recent update from the same authors compared emergency department care of pregnant women with asthma from 1996–2001 to 2001–2012 [21]. They demonstrated that treatment with OCS increased from 51% to 78% and that the prescription of OCS at discharge rose

from 42% to 63% over this time period, indicating a recent improvement in emergency department management of asthma exacerbations during pregnancy [21].

Recent data from a relatively small retrospective study of 39 women showed that pregnant women with asthma (n=28) were less likely to be prescribed OCS at the time of exacerbation (83%) than nonpregnant women with asthma (n=19, 100%) and where OCS were not prescribed at the first medical encounter, there was a delay in their prescription of 5.8 days [22]. OCS were prescribed during 87.5% of first-trimester exacerbations but only 70.6% of second-trimester and 66.7% of third-trimester exacerbations. While this may indicate an increasing reluctance to prescribe steroids as pregnancy progresses, it is possible that the severity of exacerbations in the third trimester was different from exacerbations earlier in pregnancy. This study also found that pregnant women were equally likely to fill their OCS prescription in the community after exacerbation (65%) as the nonpregnant women (67%), implying that the change in OCS use in pregnancy may be more related to prescribing habits than reduced use by pregnant women themselves, consistent with studies performed in the emergency department setting.

Intensive care management of status asthmaticus during pregnancy

There is limited literature available regarding the management of pregnant women with asthma in intensive care. A recent review suggests that multidisciplinary intensive care unit (ICU) care involving intensivists, asthma specialists, neonatologists and specialist high-risk obstetricians for pregnant women with status asthmaticus can result in good outcomes for both mother and baby, even when intubation is necessary [23]. Women whose asthma does not respond to or worsens despite maximal bronchodilator therapy in the emergency or hospital setting should be considered for ICU admission [23]. A series of five cases of status asthmaticus in pregnancy was reported from an inner city hospital in New York, NY, USA, in 2008 [24]. Three cases occurred early in pregnancy (6 weeks, 9 weeks and 14 weeks gestation), with the other two later in pregnancy (27 weeks and 28 weeks gestation). One case occurred in a woman with mild persistent asthma, highlighting the risk of severe exacerbations in pregnancy, even in those with previously mild disease. She developed severe respiratory distress and was placed on mechanical ventilation for 8 days. One woman had two admissions to the ICU, at 28 weeks and 34 weeks gestation. The second time, she was in respiratory distress and required continuous nebulised β -agonist, along with monitoring for potential respiratory failure. Her situation deteriorated on the fourth

day, and a caesarean section was performed, with bronchospasm improving significantly after delivery. In all cases presented, there were no adverse perinatal outcomes (one pregnancy was terminated at 6 weeks). The importance of prevention of severe asthma exacerbations during pregnancy and slowing their progression to status asthmaticus is emphasised [23].

Multidisciplinary approaches to the management of asthma in pregnancy

A multi-disciplinary management approach is recommended during pregnancy [5]. There are several healthcare professionals that are well positioned to offer asthma self-management education and to co-ordinate management of asthma during pregnancy. These include nurses, asthma educators, pharmacists, midwives and primary care physicians. In addition, obstetricians and respiratory specialists may be involved in antenatal asthma management.

Nurse-led approaches

In 2005, data from Australia demonstrated the potential for nurses to improve health and self-management among pregnant women with asthma [9]. At their initial visit with an asthma nurse educator (at 20 weeks gestation), pregnant women with asthma had poor adherence (40% self-reported nonadherence with ICS), poor knowledge about asthma medications (42% were inadequate) and poor device technique (16% had inadequate inhaler technique). Following education, there were improvements in all aspects of asthma self-management, such that nonadherence fell to 21% and inadequate inhaler technique to 4%. In women classified as having severe asthma, night-time symptoms and reliever medication use were significantly reduced after education [9]. This study was not powered to investigate changes in exacerbations or perinatal outcomes; however, another Australian randomised controlled trial (RCT) is proposed that plans to test a similar approach in 378 women, involving a nurse-led intervention in the antenatal clinic setting with exacerbations as the primary outcome [25].

Pharmacist-led approaches

LIM *et al.* [26] recently published a RCT testing a multidisciplinary asthma management strategy against usual care in 60 pregnant women with asthma, who were recruited prior to 20 weeks' gestation. The monthly intervention involved visits to a pharmacist who provided education about self-management strategies, monitored asthma control and consulted with the woman's

GP when step-up of ICS therapy was required. The intervention group had a statistically and clinically significant improvement in asthma control after 6 months; however, this was potentially very late in pregnancy or *post partum*, and no changes in asthma control were observed between groups at the more clinically relevant time-point of 3 months post-randomisation [26].

Involvement of midwives in antenatal asthma management

While international guidelines suggest that management of asthma during pregnancy should be multidisciplinary, very few studies have investigated the role of the midwife in antenatal asthma management, despite their primary care role in many countries. A qualitative, descriptive study has been undertaken in Australia to explore midwives' knowledge and understanding of asthma during pregnancy, and their perceived role in this area [27]. Data published to date indicate that midwives identify many barriers that prevent them from participating in antenatal asthma management, including lack of time, lack of knowledge about asthma during pregnancy, and lack of available equipment and referral pathways for women with asthma. Issues such as lack of time and knowledge are common barriers for midwives when faced with the implementation of additional education strategies for issues such as oral health, antenatal depression, genetic counselling and smoking cessation. Further research is needed to determine the importance pregnant women with asthma place on various caregivers during their pregnancy and who they would like to be providing asthma management. A study from the USA found that many women were likely to continue their ICS medication if advised to do so by their obstetrician [28], indicating the potential importance obstetric caregivers have in influencing women's health behaviours surrounding asthma during pregnancy.

Dietary approaches

GRIEGER *et al.* [29] have proposed that some of the poor perinatal outcomes associated with maternal asthma may be driven by increased oxidative stress as a result of both pregnancy and asthma. In non-pregnant adults, dietary intervention studies have demonstrated the protective effects of antioxidants in asthma; however, these approaches are yet to be tested in pregnancy. Observational data indicate that pregnant women with moderate or severe asthma have alterations in circulating antioxidants including α -tocopherol and total carotenoids, compared to women with mild or no asthma, and low concentrations were associated with reduced fetal growth [30]. Further work is required to determine whether dietary approaches can improve maternal and fetal outcomes in women with asthma.

Smoking cessation for pregnant women with asthma

Smoking is a critical issue for pregnant women with asthma, with data showing that women who smoke are more likely to have exacerbations during pregnancy and to have more severe symptoms during exacerbation [14]. Studies from around the world have suggested that pregnant women with asthma are more likely to smoke than pregnant women without asthma [15]. The 20–30% of women with asthma who continue to smoke during pregnancy are at increased risk of poor perinatal outcomes from the combined effects of smoking, asthma and severe asthma exacerbations. However, no studies have trialled smoking cessation strategies among this population of women.

A recent study from Denmark has identified the effects of both active smoking and passive smoking on asthma control [31]. Of the 500 women in this study, 6.4% were current smokers and 23% were ex-smokers, most of whom had quit smoking upon becoming pregnant. Of those who had never smoked, 18.4% reported passive smoking; that is, they lived with someone who smoked at home. Overall, those who had ever smoked had reduced lung function compared to never-smokers, while the effects of passive smoking among never-smokers showed similar patterns, with significantly reduced lung function, greater requirements for ICS and a higher likelihood of partly or uncontrolled asthma, compared to never-smokers without passive exposure [31]. These data suggest that passive smoking is potentially contributing to worse asthma control during pregnancy, which could have negative impacts on perinatal health.

Experiences of pregnant women in relation to asthma management in pregnancy

Two studies have examined the perspective of pregnant women in relation to their asthma and asthma care during pregnancy. LIM *et al.* [32] conducted qualitative interviews with 23 pregnant women with asthma in Australia, at various stages of their pregnancy or up to 5 weeks *post partum*. Some women expressed the view that there were risks associated with asthma medication use during pregnancy, particularly related to steroid use, and they were therefore cautious about using ICS unless “desperate”. Their views about the safety of reliever medication such as salbutamol were quite different, however, with women preferring to use a lot of reliever therapy rather than preventers. There were also women who were more concerned about the possible risks of uncontrolled asthma and whether the

baby was receiving enough oxygen. In terms of management by health professionals, the women noted that their GP was not concerned about their asthma and that other issues with the pregnancy often took priority. In addition, there was a view that there was a lack of information given about asthma during pregnancy, and that doctors and pharmacists were unclear about the safety of medication use in pregnancy, forcing some women to make a decision for themselves or consult “Dr Google”, where they obtained unreliable or inaccurate information [32].

A similar qualitative study was reported from the UK, in which seven women with asthma who had been pregnant within the previous 2 years were interviewed [33]. Four of these seven women reported a worsening of asthma symptoms during pregnancy, and these women expressed feelings of fear, panic and anxiety surrounding exacerbations, and a lack of understanding that some of their symptoms were due to asthma rather than the pregnancy itself. They expressed the need for more education and information so that they would have an awareness of the potential seriousness of asthma, and where to seek help. There was a lack of understanding about asthma medications and how they worked, as well as whether they were safe to use, by both women and their partners, which led to women “getting on with it” without support or assistance. This series of interviews conducted in 2012 identified that women generally did not have regular contact with GPs or practice nurses about their asthma and that management plans to monitor asthma during pregnancy were not in place, with one woman describing that her GP took her off her medication when she expressed concern about using it while pregnant. The perception was that midwives did not know much about asthma and concentrated more on issues surrounding the pregnancy. In addition, two women described delays in obtaining care when they had exacerbations of asthma requiring admission to hospital [33]. More work is needed to clarify the priorities of pregnant women themselves with regard to their asthma management in pregnancy.

The importance of active management for better maternal and fetal outcomes

The provision of optimal asthma management is essential for the health of both mother and baby. A recent systematic review and meta-analyses summarised the literature concerning the risks of adverse perinatal outcomes in women with asthma [34–36]. Compared to pregnant women without asthma, women with asthma are at risk of a range of adverse pregnancy outcomes affecting the mother, placenta and neonate,

including preterm delivery, low birth weight, pre-eclampsia [34], gestational diabetes, caesarean section, placenta praevia [36], congenital malformations, neonatal hospitalisation and neonatal death [35]. Despite the fact that the majority of women included in the primary studies would be expected to have mild asthma, the effect of asthma on perinatal outcomes was still significant, suggesting that there may be a greater adverse effect among the subgroup with more severe disease [37]. Indeed, women with moderate or severe asthma were more likely to have small for gestational age babies than women with mild asthma [16]. Another interesting finding of this review was that active management of asthma during pregnancy may mitigate some of the increased perinatal risks. In the meta-analysis, when studies were grouped based on the provision of active asthma management, the risk associated with maternal asthma was reduced to nonsignificant for some perinatal outcomes. For example, women with asthma had a 50% increased risk for preterm delivery compared to women without asthma when no active management was given [34]. However, among five studies where active management was provided, the risk of preterm delivery was no longer increased or statistically significant, suggesting that active asthma management may be effective in reducing the risk of preterm delivery [34]. Similar results were observed for preterm labour [34] and neonatal hospitalisation [35]. The reduced risk of neonatal hospitalisation may be a consequence of improvements in gestational age and other birth outcomes. A reduction in preterm births with active asthma management is plausible, given that one of the benefits would be a reduction in the number of exacerbations and courses of oral steroids used, both of which have been implicated in larger studies as contributing to the risk of preterm delivery in asthmatic women.

Interventions for improving asthma management during pregnancy

There have been very few recent RCTs of interventions for managing asthma during pregnancy. A 2014 Cochrane review summarised eight RCTs involving 1181 women with asthma [38]. Five of the trials assessed pharmacological interventions and three assessed nonpharmacological interventions. The trials were of moderate quality overall and did not lead to any firm conclusions regarding optimal asthma management in pregnancy, due to a lack of clear benefits of pharmacological approaches over current practice and a lack of power in the nonpharmacological interventions to detect differences in perinatal outcomes [38].

Educational questions

- Which of the following statements concerning guidelines for the management of asthma during pregnancy is/are correct?
 - Inhaled corticosteroids should be used when women have persistent asthma
 - Asthma should be managed as for other adults, with the exception of oral corticosteroid use during exacerbations
 - Multidisciplinary management is recommended
 - It is important to identify and manage comorbid conditions such as rhinitis or reflux
 - Asthma should be reviewed every 4 weeks during pregnancy.
- A woman presents to her general practitioner with asthma symptoms during pregnancy. She has previously admitted to nonadherence to her preventer medication and is concerned about whether this medication is harmful for her baby. Which is the most appropriate clinical decision?
 - Withdraw all preventer medication and advise her to take more doses of her reliever
 - Make a referral for her to see a respiratory specialist
 - Advise her of the safety and importance of taking preventer medications in pregnancy, and advise her to continue her prescribed dose and return for review if symptoms continue to worsen
 - Perform spirometry and provide a prescription for a different preventer medication
- Which of the following statements is/are true concerning the risks of adverse perinatal outcomes in women with asthma?
 - Women with asthma are not at risk of adverse perinatal outcomes compared to women without asthma
 - Women with asthma are at increased risk of having a baby who dies or is hospitalised after birth
 - Active management of asthma can reduce the risk of preterm labour and delivery
 - Women who have exacerbations of asthma during pregnancy are at three times the risk of low birth weight compared with women without asthma exacerbations in pregnancy
- Which of the following statements is/are true concerning inflammation-based management of asthma during pregnancy?
 - Using a marker of airway inflammation to adjust treatment results in women taking higher doses of inhaled corticosteroids during pregnancy
 - Using a marker of airway inflammation to adjust treatment reduces the exacerbation rate in pregnancy
 - Exhaled nitric oxide fraction is a useful marker because it predicts the response to inhaled steroids
 - Benefits to health in infancy have been described when inflammation-based management is used
 - No studies have identified whether this approach improves perinatal outcomes.

Inflammation-based management of asthma during pregnancy

Only one study has successfully trialled a management approach that reduces exacerbations during pregnancy. The MAP (Managing Asthma in Pregnancy) Study from Australia was a double-blind, parallel-group RCT which tested the

efficacy of an inflammation-based management strategy for reducing exacerbations in 220 non-smoking pregnant women with asthma [39]. Women were randomised prior to 22 weeks gestation. The control group had treatment adjusted according to the results of the Asthma Control Questionnaire (ACQ), representing symptoms and lung function. The intervention group had treatment adjusted according to both the level of eosinophilic airway inflammation and the ACQ. Airway inflammation was measured by exhaled nitric oxide fraction (F_{eNO}), a steroid sensitive marker of eosinophilia, and used to adjust ICS. The ACQ was used to determine when symptoms remained uncontrolled, in which case a LABA was added. Both groups had stepwise ICS treatment adjustments (up or down) made monthly, and received free medications and self-management education. The primary study outcome was exacerbations requiring medical intervention, defined as hospitalisation, emergency department presentation, use of OCS or unscheduled doctor visit for asthma. There was a 50% reduction in exacerbations in the F_{eNO} group compared to the control group, along with alterations to the treatment profile, with more women from the F_{eNO} group being prescribed ICS (at a lower mean dose) and ICS/LABA combination therapy. In addition, there was a significant reduction in both OCS and SABA use, and a significantly higher quality of life in the F_{eNO} group compared to the control group [39]. The infants from this study were followed up at 12 months of age and those from mothers in the F_{eNO} group were significantly less likely to have recurrent

bronchiolitis or recurrent croup reported by their parents [40], suggesting a potential long-term benefit to the health of the offspring. The F_{eNO} -based management approach has the potential to be widely used in clinical practice, as F_{eNO} is easily measured using a noninvasive breath test and gives an indication of the level of steroid-responsive eosinophilic airway inflammation, reducing exacerbations, a major clinical problem in pregnant women with asthma.

Conclusions

Asthma is a common comorbidity during pregnancy and exacerbations are a major clinical problem, with up to 45% of women requiring medical intervention for asthma during pregnancy, resulting in poor outcomes for mothers and their babies. Guidelines recommend managing asthma actively during pregnancy, with regular 4-weekly review, provision of a written action plan, use of preventer medications as indicated for adults and management of comorbid conditions. Improvements have been made in recent years in emergency department management of asthma in pregnancy, and multidisciplinary approaches are being proposed to optimise both asthma outcomes and perinatal outcomes. One strategy that has been successful in reducing exacerbations in pregnancy is treatment adjustment using a marker of eosinophilic lung inflammation, F_{eNO} . Further evidence is needed to determine whether this strategy can also improve perinatal outcomes and be successfully translated into clinical practice.

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Conflict of interest

None declared.

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Suggested Answers

1. a, c, d, e
2. c
3. b, c, d
4. b, c, d, e

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