

Editorial

Long-term benefits of optimal asthma control in pregnancy

Diane R. Gold, MD, MPH,^{a,b} and Augusto A. Litonjua, MD, MPH^b Boston, Mass

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The benefits to both the mother and newborn of actively controlling asthma symptoms during pregnancy have been shown to “markedly outweigh any potential risks of usual controller and reliever medications,” according to the “Global Strategy for Asthma Management and Prevention” (Global Initiative for Asthma [GINA]) 2017 update.¹ In that update GINA cites evidence for these benefits and provides recommendations for active asthma management during pregnancy, emphasizing the need to step up medication treatment if asthma is not well controlled and the need to be cautious about stepping down treatment if asthma is under good control. Poorly controlled maternal asthma is associated with increased risk of placental insufficiency, maternal and fetal hypoxia, perinatal mortality, pre-eclampsia, preterm birth, and low birth weight; better asthma control markedly decreases the risk.^{2-4,E1,E2}

In their study linking the Danish national registries, which was published in this issue of the *Journal*, Liu et al⁵ suggest that optimal maternal asthma control in pregnancy might extend beyond neonatal outcomes and include reduction of both transient wheezing and early-onset persistent childhood asthma. The study, which links records of asthma medication prescription to diagnostic and health care use records, has limitations and strengths associated with the use of administrative data. The information about asthma control measures during pregnancy was limited, and the authors were not able to determine which trimester was affected. Furthermore, there is uncertainty about the relative contribution of inheritance, maternal asthma phenotype at baseline before pregnancy, common environmental exposures, and suboptimal asthma management to worsen wheeze or long-term asthma outcomes for offspring. The authors cite literature that has associated preterm birth or lower birth weight not only with asthma exacerbations in pregnancy but also with increased wheeze or asthma in early childhood. However, they were not able to determine whether gestational age or low birth weight

mediated the relation of maternal asthma control with child asthma risk in their cohort.

Nevertheless, their study adds to the literature supporting the GINA and National Asthma Education and Prevention Program (NAEPP) guidelines and advice to intensify support of women with asthma during pregnancy.^{1,3,4} All pregnant women with active asthma, including those whose symptoms are under good control, should be actively monitored. However, new data challenge older studies that concluded that the course of asthma in pregnancy is entirely unpredictable (eg, one third get better, one third get worse, and one third stayed the same).^{E3} Women with persistent symptoms and difficult-to-control asthma before pregnancy are at particular risk for asthma exacerbations once pregnant.^{2,E4}

The mechanisms for the influences of pregnancy on asthma⁶ are only partially understood. Pregnancy can increase chest wall or diaphragmatic restriction and gastroesophageal reflux, and these physiologic changes, particularly when accompanied by obesity and excessive weight gain, might worsen asthma symptoms, even if they do not worsen airflow obstruction. Obesity-associated airway inflammation can worsen both asthma control and sleep apnea, and the 2 processes might be interrelated. The hormonal changes of pregnancy have been hypothesized to influence both conditions, but their effects on asthma in pregnancy are uncertain, despite growing evidence that apart from pregnancy, sex hormones can influence asthma. Pregnant women might also be at higher risk of viral respiratory tract infections, including influenza, perhaps because of functional immune changes that protect against fetal rejection. Hay fever/allergic rhinitis might compound the perception of dyspnea that occurs with pregnancy and asthma and might be accompanied by lower airway inflammation. Maternal stress, depression, or anxiety can also worsen prenatal asthma control and have been linked not only to adverse maternal but also adverse child outcomes, including lower birth weight and childhood wheeze, allergy, and asthma.²

Guidelines for asthma management, which are far more comprehensively presented in editorial references, include regular monitoring for symptoms and lung function (peak flow, spirometry, or both) throughout pregnancy. In addition, recent literature suggests the potential contribution of monitoring exhaled nitric oxide levels in adjustment of ICS dosing.^{2,E5} Usual treatment with inhaled controller and reliever medications is recommended, according to the NAEPP or GINA step-up guidelines, and step up should occur when asthma symptoms are not under good control. Medication prescriptions should be accompanied by best-practice asthma education in inhaler technique and compliance with medications, with reassurance that there is little to no risk from the usual doses of inhaled short- or long-acting β -agonists or inhaled corticosteroids,⁷ which can protect against the known risks of asthma exacerbations.⁶ When maximal therapy with the usual inhaled medications does not control symptoms and airflow obstruction, oral/systemic corticosteroids should be

From ^athe Channing Division of Network Medicine, Brigham and Women's Hospital, Harvard Medical School, and ^bthe Department of Environmental Health, Harvard T.H. Chan School of Public Health.

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Corresponding author: Augusto A. Litonjua, MD, MPH, Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115-5804. E-mail: augusto.litonjua@channing.harvard.edu.

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Box 1. Social, cultural, and economic determinants of good asthma control in pregnancy

- Affordable health care and asthma medications
- Access to health care
- Access to healthy housing and healthy, safe neighbourhoods
- Excellent asthma education, sensitive to culture and language

used with careful monitoring. Particularly in the first trimester of pregnancy, systemic corticosteroid use is associated with increased risk of cleft lip or cleft palate (from 0.1% in the normal population to 0.3% in women receiving oral corticosteroids)³ and also associated with impaired glucose control, low birth weight, preterm birth, pre-eclampsia, and intrauterine growth restriction,⁸ although with some of these outcomes, it can be difficult to disentangle the effects of poor asthma control from the effects of oral corticosteroids. Anaphylaxis to the steroid-sparing anti-IgE biologic omalizumab is rare but can occur.^{E6} Although there is no evidence to date that patients whose severe persistent allergic asthma symptoms are well controlled with omalizumab⁹ or other steroid-sparing biologics should stop their therapy once pregnant, studies on these relatively new agents are small, and the US Food and Drug Administration encourages postmarketing reporting of any adverse effects.

With a number of caveats related to animal data and limited human data demonstrating the risk with specific classes of medications (particularly in the first trimester), guidelines also recommend treatment of conditions that might worsen asthma control, including gastroesophageal reflux and allergic rhinitis. Nonpharmacologic treatment (eg, saline lavages) and trigger avoidance are encouraged more than medications for rhinitis.⁸ According to the NAEPP guidelines and review of US Food and Drug Administration findings on human and animal toxicological findings, oral and nasal decongestants should be avoided. Oral antihistamines should be used cautiously, even after the first trimester, because human data supporting their safety are limited.⁸ Influenza vaccine, which has a reassuring safety record in pregnancy,^{E7} is strongly recommended, as is avoidance of known environmental triggers (eg, tobacco smoke or cat, dog, cockroach, or mouse for those with specific allergic sensitization).

Best asthma management practice in pregnancy, including asthma education, needs to address the woman's economic, cultural, and psychosocial realities (Box 1). Even in Denmark, where health equity is a cornerstone of its universal health care system, concerns about increasing health disparities have resulted in recommendations for policies to improve access to care.¹⁰ In

the urban US setting, often the most vulnerable and disadvantaged populations are at highest risk of poor asthma control in pregnancy. Women might not have prenatal care at all or might seek both asthma and prenatal care in the third trimester.

When a woman presents for or is offered prenatal care, if she has active asthma, it is important to evaluate whether instructions on inhaler use have been adequately communicated and reinforced. Can she afford her inhalers, and if not, how can economic barriers be overcome? Is trigger avoidance possible? What is her housing situation, and can it be improved, including both stress and other environmental trigger reduction? In the best of all social and economic situations, only a very small proportion of pregnant women with active asthma would require oral corticosteroids; most would have good asthma control. Then we should be able to evaluate the extent to which asthma risk in offspring can be decreased by maximizing control of asthma while also globally improving quality of life in pregnancy.

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