Perinatal complications associated with maternal asthma during pregnancy

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Summary

Background: Asthma is one of the most common medical illnesses occurring in pregnancy and its incidence amongst the obstetric population is increasing. Previous studies have suggested that asthma is not a benign illness in pregnancy, and can contribute towards increased rates of pregnancy complications.

Methods: We undertook a retrospective audit of 6458 deliveries during 2008 at The Royal Women's Hospital to determine the perinatal outcomes for women with a self-reported diagnosis of asthma.

Results: We found that 501 (7.8%) deliveries were to women who identified themselves as asthmatics. Of these, 15.6% reported exacerbations of their asthma symptoms during pregnancy, with the remainder reporting improvement or stabilization. There was an increased rate of preterm birth (12.9%) in the asthmatic population, compared to the non-asthmatic population (OR = 1.48, CI [1.12–1.95], $P = 0.005$). Asthma remained significantly associated with an increased risk of preterm birth after adjusting for maternal smoking status using logistic regression analysis (Adjusted OR 1.41, CI [1.07–1.86], $P = 0.01$). Women were also at increased risk of developing pre-eclampsia (OR 1.71, CI [1.09–2.67], $P = 0.02$) but not fetal growth restriction. Women identifying themselves as asthmatics were also more likely to deliver by caesarean section (OR 1.32, CI [1.09–1.6], $P = 0.003$).

Conclusion: These findings suggest that maternal asthma may be associated with an increased risk of preterm birth, pre-eclampsia and caesarean delivery.

Keywords: asthma, pregnancy, pre-eclampsia, preterm birth, caesarean section

INTRODUCTION

Asthma is one of the most common medical illnesses occurring in pregnancy. The incidence of asthma is increasing, with 3–12% of pregnant women identifying themselves as asthmatics.¹ Several studies have suggested that asthma is not a benign illness in pregnancy, with an increased incidence of preeclampsia^{2,3}, preterm birth⁴, infants with low birth weight or intrauterine growth restriction (IUGR) and perinatal death noted in the asthmatic population.^{5,6} Some studies, however, have failed to confirm such associations.^{7–9} Although it is thought that asthma exacerbations may contribute towards these risks, the role of such exacerbations is poorly defined.

The effect of pregnancy on asthma is variable. It has been suggested that during pregnancy approximately one-third of women experience an exacerbation of asthma symptomatology, one-third have no change to their asthma, and one-third have improvements in their asthma symptoms.^{1,10,11} The acute effects of an asthma exacerbation include the potential reduction in oxygen supply to the fetus,¹² while the chronic

effects of uncontrolled asthma on pregnancy are multiple, including increased maternal morbidity and mortality due to a loss of asthma control.¹⁰

The results of these studies suggest that asthma can potentially complicate or be complicated by pregnancy. We undertook a retrospective audit to determine the pregnancy outcomes for asthmatic women delivering at The Royal Women's Hospital, Melbourne.

METHODS

A retrospective analysis of medical records for women who delivered at The Royal Women's Hospital in 2008 was undertaken. Women who identified themselves as asthmatics during their pregnancy were included in the study group. This study was approved by the Human Research Ethics Committee as a quality assurance audit.

Information was collected regarding maternal demographics including gravidity and parity, maternal age at delivery, body mass index at initial antenatal visit, smoking status of the patient and her partner and pre-existing medical diagnoses. Antenatal records, emergency department records and admission histories were examined for evidence of the use of asthma medications and asthma exacerbations occurring

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during pregnancy, as well as pregnancy complications prior to and/or impacting upon delivery. Information regarding the gestation and mode of delivery was extracted, as was the infant's birth weight, sex, Apgar scores and details concerning neonatal nursery admissions.

The Australian national birth weight percentiles by gestational age charts (Roberts and Lancaster) were used to classify infants as small for gestational age (SGA). Data concerning the non-asthmatic population of women who delivered at the Royal Women's Hospital for 2008 were gathered from the birthing statistics database.

Statistical analyses

Continuous data were compared using Student's *t*-test and categorical data were compared using Pearson's chi-squared statistic. Logistic regression was used to investigate the effect of confounders including maternal smoking status. All analyses were performed using Stata 7.0 (Stata Corporation LP, College Station, TX, USA).

RESULTS

There were 6458 eligible deliveries at the Royal Women's Hospital in 2008; 501 of these women identified themselves as having a medical diagnosis of asthma and were included in this study, while 5957 patients were included in the non-asthmatic subgroup. Demographic information regarding maternal age at delivery and parity was very similar between the two groups (Table 1). Of note, 23.4% of the women who identified themselves as asthmatics were smoking during their pregnancy, compared with 12.1% of the non-asthmatic population ($P < 0.001$). Of those in the asthmatic population who stated they were non-smokers ($n = 384$), 75 had a partner who smoked. Hence 192 (38.3%) pregnancies in the asthmatic population were exposed to cigarette smoke.

Mode of delivery

Overall, the rate of caesarean section was significantly increased in the asthmatic group compared with the non-asthmatic group

(odds ratio [OR] 1.32, confidence interval [CI] [1.09–1.6], $P = 0.003$). Emergency caesarean sections were more common among asthmatics while elective caesarean sections were less common, although this did not achieve statistical significance. There were no statistically significant differences in the indications for emergency caesarean sections between the asthmatic and non-asthmatic women. Rates of vaginal delivery and operative vaginal delivery were similar between the two groups.

Medication use

A total of 52.7% of the women who identified themselves as asthmatics reported using asthma medication on either a regular or as required basis. Salbutamol was the most common asthma medication, with 32.7% of asthmatics using salbutamol alone. Eighty-five patients (16.9%) used inhaled corticosteroids (predominantly Budesonide). All these patients were advised to continue this medication throughout the pregnancy; however, compliance was not formally documented. Interestingly, 47.3% of patients who identified themselves as asthmatics stated that they did not use asthma medications. No patients required chronic oral corticosteroid therapy.

Asthma exacerbations

The majority of the asthmatic women had no asthma exacerbations recorded during their pregnancy ($n = 422$, 84.2%), while 79 women (15.8%) had worsening of their asthma symptomatology. Despite this, less than half ($n = 38$) changed their asthma management regimen. Of those who reported that their asthma management had changed, 27 were managed as an outpatient, seven presented to an emergency department (of whom two required treatment with short-term oral corticosteroids) and four were admitted for inpatient stabilization (which included treatment with oral corticosteroids). No patients required admission to the high dependency or intensive care units for management of their asthma.

The frequency of asthma exacerbations appeared to increase throughout the pregnancy with 13.9% occurring in the first trimester, 36.7% in the second and 49.4% in the third.

Table 1 Demographic data

	Asthmatic population, $n = 501$	Non-asthmatic population, $n = 5957$
Maternal age at delivery: Mean $\pm$ SD	29.7 $\pm$ 6.0	30.9 $\pm$ 5.58
Primigravidae, n (%)	253 (50.5%)	3506 (51.2%)
Smoking status (at <20 weeks gestation)		
Smoker, n (%)	117 (23.4%)	720 (12.1%)
Non-smoker, n (%)	384 (76.6%)	5237 (87.9%)
Gestation at delivery (weeks): Mean $\pm$ SD	38.8 $\pm$ 3.2	38.7 $\pm$ 2.8
Mode of delivery		
NVD, n (%)	258 (51.5%)	3275 (55.0%)
Operative vaginal delivery, n (%)	54 (10.8%)	807 (13.5%)
Caesarean section, n (%)	189 (37.7%)	1875 (31.5%)
Elective, n (%) of total caesarean sections	63 (33.3%)	695 (37.0%)
Emergency, n (%) of total caesarean sections	126 (66.7%)	1180 (63.0%)
Indication for emergency caesarean section		
Non-reassuring fetal status	63 (50.0%)	574 (48.6%)
Malpresentation	11 (8.7%)	100 (8.5%)
Labour dystocia	36 (28.6%)	342 (29.0%)
Other	16 (12.7%)	164 (13.9%)
Anaesthesia for all caesarean sections (elective and non-elective)		
Regional (spinal/epidural)	172 (91.0%)	1739 (92.7%)
General anaesthetic	17 (9.0%)	136 (7.3%)

NVD = normal vaginal delivery

Obstetric complications

Preterm birth, defined as delivery prior to 37 completed weeks gestation, was the most common pregnancy complication affecting the asthmatic population with 12.9% of the asthmatic mothers delivering preterm, compared with 9.2% of the non-asthmatic population. This was statistically significant (OR = 1.48, CI [1.12–1.95], $P = 0.005$). The incidence of preterm birth in women who smoked in the asthmatic population was also higher (33.8%) than the incidence of preterm birth for women who smoked in the non-asthmatic population (15.6%). After adjusting for maternal smoking status using logistic regression, asthma remained significantly associated with an increased risk of preterm birth (adjusted OR 1.41 [1.07–1.86], $P = 0.01$).

Preeclampsia was also seen significantly more commonly in the asthmatic women (4.59%) compared with the non-asthmatic women (2.84%, OR 1.71, CI [1.09–2.67], $P = 0.02$).

Neonatal outcomes

Multiple pregnancies were included in these data with 522 and 6103 infant outcomes analysed for the asthmatic and non-asthmatic groups, respectively (Table 2).

Perinatal mortality was very low and similar between both the asthmatic and the non-asthmatic populations (1.3% and 1.5%, respectively). Eighty-three (15.9%) infants born to asthmatic women and 803 (13.2%) infants born to non-asthmatic women were classed as SGA. Although there was a trend towards SGA being more common among asthmatic women, this did not reach statistical significance. Further stratification revealed no difference in the subgroups of infants weighing <5th centile between both the asthmatic and non-asthmatic women (4.6% and 3.5%, respectively). Moreover, we did not observe any sex differences in the proportion of infants with SGA in each group (54.2% male in the asthmatic versus 55.0% male in the non-asthmatic population).

DISCUSSION

Asthma is a common medical illness with 7.8% of women delivering at The Royal Women's Hospital in 2008 identifying themselves as asthmatics. These figures are consistent with those from other centres,¹ which confirm that asthma is becoming more prevalent in obstetric populations. This study identified that women with asthma were more likely to have a preterm birth and to deliver by caesarean section. A recent large meta-analysis by Murphy *et al.*¹³ has also indicated that pregnant women with asthma are at a significantly increased risk of multiple adverse perinatal outcomes, including low birth weight, SGA, preterm labour and delivery, and preeclampsia.

This study involved the retrospective analysis of medical records and as such is subject to several limitations. It is possible that the prevalence of asthma may have been overestimated, as it relied upon the self-reporting of a diagnosis of asthma rather than accurate medical verification.

We were unable to investigate asthma severity prior to pregnancy. Our data relied on patients' self-reporting of their medical history. Information regarding smoking behaviours, medication use and asthma exacerbations outside of antenatal visits, and hospital admissions may be subject to underreporting due to patient recall and limited documentation by medical staff. Nevertheless, despite these limitations, this large data-set provides important insights into the potential increased risks during pregnancy of this common medical condition.

It is well known that smoking is associated with low birth weight, preterm delivery, premature rupture of membranes and a reduced incidence of preeclampsia.¹⁴ Given this, and the high incidence of asthmatics who are also smokers in our study, we acknowledge that smoking is a likely confounder in adverse pregnancy outcomes, as well as a potential trigger for asthma exacerbations. Also, given that almost half (47.3%) of the women who identified themselves as asthmatics do not use asthma medications, we query the accuracy of the patient's diagnosis of asthma. It is possible that deteriorations in respiratory function due to smoking could resemble the symptoms of an asthma exacerbation.

Mode of delivery

Patient demographic characteristics were very similar between the asthmatic and non-asthmatic populations, but the rate of caesarean section was significantly increased in the asthmatic population compared with the non-asthmatic population (OR 1.32, CI [1.09–1.6], $P = 0.003$). There were more emergency caesarean sections in the asthmatic population, although this was not statistically significant. Sheiner *et al.*¹⁵ reported higher rates of caesarean deliveries among asthmatic patients compared with controls (17.1% versus 11.4%, $P < 0.001$) and that this association persisted after controlling for possible confounders such as failure to progress in labour, malpresentations and IUGR. Asthmatic patients may have greater exposure to medical practitioners because of their asthma, and closer observations may lead to increased recognition of medical complications leading to caesarean section.

Smoking

Over 23% of the women who identified themselves as asthmatics in our study were smokers. Smoking prevalence during pregnancy may be difficult to discern; most studies

Table 2 Perinatal outcomes

	Asthmatic population (<i>n</i> = 522)	Non-asthmatic population (<i>n</i> = 6103)	Odds ratio	<i>P</i> value
Perinatal mortality, <i>n</i> (%)	7 (1.3%)	90 (1.5%)	0.91	$P = 0.81$
Neonatal death, <i>n</i> (%)	5 (1%)	27 (0.4%)	2.18	$P = 0.1$
Stillbirth, <i>n</i> (%)	2 (0.4%)	63 (1%)	0.37	$P = 0.15$
SGA <10th centile, <i>n</i> (%)	83 (15.9%)	803 (13.2%)	1.25	$P = 0.08$
SGA <5th centile, <i>n</i> (%)	24 (4.6%)	216 (3.5%)	1.31	$P = 0.21$

SGA, small for gestational age

rely on self-reported smoking behaviours and are therefore subject to under-reporting. The Australian Institute for Health and Welfare's National Perinatal Data Unit reports that in 2005, 17.4% of women smoked during pregnancy.¹⁶ It is estimated that 22% of American women of reproductive age smoke.¹⁷

The contribution of smoking to asthma exacerbations during pregnancy remains unclear. Few studies have been able to adequately control confounding factors. Murphy *et al.*¹⁸ reported that the rate of smoking in women with a severe asthma exacerbation was similar to that in women without an asthma exacerbation (25%), while Tong *et al.*¹⁷ reported an increased rate of smoking in women who suffered an asthma exacerbation during pregnancy, although the difference was not statistically significant.

Asthma in pregnancy

In this study, 78 (15.6%) patients reported a worsening in their asthma symptoms. Those requiring admission or presentation to an emergency department for stabilization comprised 2.2% of the asthmatic population. Schatz *et al.*¹¹ found that 17% of women who felt their asthma had not changed during their pregnancy had been required to present to an emergency department, and 2% were admitted. In a subsequent study, Schatz *et al.*¹⁹ noted that as many as 20% of women had asthma exacerbations during pregnancy requiring medical attention, even in those with actively managed asthma.

Whether asthma exacerbations reflect asthma severity, non-compliance or increased exposure to external triggers remain unclear. Our results indicate that many women identifying themselves as asthmatics do not take asthma medications and hence may render themselves more susceptible to asthma exacerbations. Some women may cease their usual asthma medication during pregnancy for fear it will detrimentally affect their pregnancy, resulting in suboptimal treatment.

Preeclampsia

Previous studies investigating a relationship between asthma and preeclampsia have produced varying results. Steinius-Aarniala *et al.*²⁰ reported a three-fold increased risk of mild preeclampsia in women hospitalized for asthma, compared with women who did not have an exacerbation. However, a larger study suggested that asthma exacerbations had no effect on preeclampsia.² Our data suggest that women who identify themselves as asthmatics are at a moderately increased risk of preeclampsia. While the majority of women diagnosed with preeclampsia in our asthmatic population reported no worsening of their asthma symptoms, some used salbutamol and inhaled corticosteroids during their pregnancy (26.3%), with 36.8% using salbutamol alone. This may indicate that women with moderate to severe asthma may be at increased risk of developing preeclampsia without obvious worsening of their asthma.

Preterm delivery

This study demonstrates that women who identified themselves as asthmatics were significantly more likely to have a preterm delivery than non-asthmatic women (OR 1.48, CI [1.12–1.95], $P = 0.005$). Bakhireva *et al.*⁴ also reported that

preterm delivery was significantly more common among patients with poor asthmatic control during the first part of pregnancy (11.4%) compared with patients with adequate asthma control (6.3%; $P = 0.02$). Murphy *et al.*,¹⁰ however, reported no significantly increased risk of preterm delivery in women who had an exacerbation of asthma during pregnancy, or in women who did not have an asthma exacerbation, compared with women without asthma. Only four (6.2%) of the women in our asthmatic population who had a preterm delivery reported an asthma exacerbation during their pregnancy.

Low birth weight

Mean birth weight has been reported to be significantly lower in infants from asthmatic mothers, compared with those without asthma.²⁰ Our study demonstrates that 15.9% of the infants born to women in our asthmatic population were classified as SGA, compared with 12.9% of our non-asthmatic population. A lower maternal FEV₁ (forced expiratory volume in 1 second) may predispose to IUGR.²⁰ A recent prospective cohort study from Australia showed that women with severe asthma exacerbations requiring medical intervention were at an increased risk of reduced male birth weight.¹⁸ The mechanisms for the effect of exacerbations on low birth weight are unknown, but may include a direct effect of fetal hypoxia on growth, or changes in fetal growth via reduced uteroplacental blood flow or other alterations in placental function.²¹

CONCLUSION

The results of this study suggest that maternal asthma is associated with an increased risk of preterm delivery, preeclampsia and caesarean section. The precise aetiology for these findings remains unclear. Antenatal consultations should provide information regarding smoking and asthma medication use during pregnancy and routinely and continuously monitor asthma symptomatology. Further research is needed to accurately assess the incidence of asthma, the role of asthma exacerbations on pregnancy outcomes and the potential contributions of asthma towards preterm delivery and preeclampsia.

DECLARATIONS

Competing interests: Nil.

Funding: Nil.

Ethical approval: This study was approved by the Royal Women's Hospital Human Research Ethics Committee (as documented in Methods section).

Guarantor: SJ.

Contributorship: SJ and JS researched literature and conceived the study. Both were involved in gaining ethical approval. SJ collected the data. JS performed statistical analyses. SJ wrote the first draft of the manuscript. Both authors reviewed and edited the manuscript and approved the final version of the manuscript.

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(Accepted 28 November 2011)