



Obstetrics and Gynaecology Cases - Reviews

Case Report: Open Access

A Case Study of Stillbirth in a Pregnancy Complicated by Asthma

Vicki L Clifton^{1,2*} and Maureen D Busuttil^{1,3}

¹Department of Paediatrics and Reproductive Health, Robinson Research Institute, University of Adelaide, Australia

²Mothers and Babies Research Centre, Hunter Medical Research Institute, University of Newcastle, Australia

³Emergency Department, Lyell McEwin Health Service, Australia

*Corresponding author: A/Professor V.L. Clifton, Department of Paediatrics and Reproductive Health, Robinson Research Institute, University of Adelaide, Medical North Building, Level 6, Frome Rd, Adelaide SA 5005, Australia, Tel: 6128 83038321, Fax: 618 83034099, E-mail: Vicki.clifton@adelaide.edu.au

Abstract

Asthma during pregnancy can be complicated by intrauterine growth restriction, preterm delivery and stillbirth. This paper reports the obstetric and respiratory history of a 23 year old woman whose pregnancy was complicated by asthma and a severe asthma exacerbation that was associated with a stillbirth at 34 weeks gestation. The article attempts to link the relationship between asthma in pregnancy and adverse fetal outcomes and therefore highlights the need for multidisciplinary care of pregnant asthmatic women and the increased need for greater awareness by health professionals and pregnant women of the use of inhaled corticosteroid (ICS) treatment during pregnancy in combination with an asthma action plan.

Background

A large North American collaborative project on asthma and pregnancy reports that there are no significant differences in perinatal outcomes between asthmatic and non-asthmatic women [1]. However, one factor that was not considered in this study was the impact of acute exacerbations on fetal outcome. Our recent studies of pregnant asthmatic women identified that those asthmatic women who experienced an acute exacerbation during pregnancy had a number of adverse outcomes including intra uterine growth restriction, preterm delivery or still birth [2-4].

In this paper the events leading to a stillbirth in a pregnancy complicated by chronic asthma and an acute exacerbation that occurred during a prospective cohort study of asthmatic women will be described [5]. The case study will highlight the importance of asthma management during pregnancy by general practitioners, obstetricians and respiratory physicians and demonstrate that asthma is a risk factor during pregnancy that should be seriously considered.

Materials and Methods

Subjects

This case was part of a prospective cohort study that was approved by the Hunter Area Health Service and University of Newcastle Human Research Ethics Committees. Pregnant women with and without asthma were recruited in the John Hunter Hospital,

Newcastle, NSW antenatal clinic during the first trimester, following a previously described protocol [5]. Clinical asthma severity was rated as mild, moderate or severe using the integrated severity score described in the Australian Asthma Management Guidelines [6], which closely approximate the National Heart, Lungs and Blood Institute Guidelines [7]. Appropriate inhaler use and compliance was assessed in the Asthma Management Service [8].

Results

Case

This is the case of a 23 year old, non-tobacco smoking, marijuana smoker with no major social problems except that her partner was unemployed. This Caucasian woman, gravidity 0, parity 0, at 34 weeks gestation presented to the Emergency Department with a severe exacerbation of asthma. She was a known asthmatic but had ceased preventer medications 2 years ago due to a reduction in her symptoms however reported that she had experienced increasing symptoms since her pregnancy. Pregnancy had been complicated with increasing reflux and heartburn although this was not disclosed in any of her antenatal visits, a mild exacerbation of her asthma at 14 weeks and anemia at 30 weeks gestation at which time she was commenced on iron replacement. The treatment that was instituted for her asthma exacerbation was not documented but her antenatal record showed the use of salbutamol on an as needed basis up to twice per day. Early gestation scan reported fetal growth was normal. Prior to her emergency presentation the patient had experienced worsening difficulty breathing and had used nebulized salbutamol in the preceding 48 hours and had used 6 x 5mg/ml salbutamol nebulizers during the morning before presenting to the emergency department. When she first presented to hospital she was noted to be hypoxic with saturations of 90% on room air. On examination she was afebrile, heart rate of 122 and blood pressure of 139/80. There was widespread audible wheeze in at inspiration and expiration and her examination was otherwise unremarkable. Her peak flow was 250 L/min. prior to administration of any treatment and was only improved to 280L/min post treatment with one salbutamol nebulization. She was considered to be too unwell to remain at the local hospital and was transferred to tertiary hospital for specialist care within the obstetric unit. The patient was admitted for treatment with intravenous hydrocortisone

Citation: Clifton VL, Busuttil MD (2015) A Case Study of Stillbirth in a Pregnancy Complicated by Asthma. *Obstet Gynecol Cases Rev* 2:027

Received: January 18, 2015; **Accepted:** March 23, 2015; **Published:** March 25, 2015

Copyright: © 2015 Clifton VL. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Table 1: Maternal characteristics of non-asthmatic and asthmatic subjects that had a live birth and case study subject who had a stillbirth

Maternal Characteristics	Control	Asthmatic	Case 1
Total number of subjects	39	184	9
Age(yrs)	28.8	26.2*	23
Standard error	0.65	0.39	
Height(cms)	164.5	164	156.5
Standard error	1.2	0.5	
Weight at beginning of pregnancy(kg)	70.2	73.8*	61
Standard error	2.8	1.6	
Weight during pregnancy(kg)	11.2	11.3	15.45
Standard error	1.1	0.5	
Gravidity	2.6	2.4*	0
Standard error	0.3	0.12	
Parity	1.2	0.9*	
Standard error	0.2	0.1	
Gestational age at delivery(weeks)	39	39.2	34
Standard error	0.6	0.2	
%predicted FEV1	96	89.6*	74
Standard error	2.5	1.6	
FEV1 VC	0.85	0.81*	0.82
Standard error	0.02	0	
Inhaled glucocorticoid intake during pregnancy			
First trimester ug/day	0	46.9*	0
Standard error		43.9	
Second trimester ug/day	0	577.2*	0
Standard error		50.7	
Third trimester ug/day	0	638.7*	1000
Standard error		51.8	
Periodic oral glucocorticoid intake during pregnancy	No	yes	yes

* $P < 0.05$ Student t-Test

and nebulized salbutamol only as frequently as every 2 hours in spite of the severity of her asthma. She was not treated with supplemental oxygen and her saturations remained low between 93 and 96%. She also was tachycardic during the first 48 hours of her admission. Fetal heart was documented but no fetal monitoring was performed. The laboratory investigations were unremarkable aside from a mild anemia with haemoglobin of 104. Ultrasound was conducted one day after admission and reported an anatomically normal, live fetus with normal umbilical artery systolic/diastolic flow (Table 1).

Prednisolone (25mg/day) and inhaled beclomethasone dipropionate (1000µg/day) was commenced on the third day of her admission in place of hydrocortisone. By the fifth day her condition had improved with her PEFr pre and post salbutamol 250/L min and 360/L min respectively. The patient was discharged from hospital after six days with continuing inhaled and oral steroid as prescribed in hospital. Fetal heart was noted but the rate not documented on discharge. The patient then returned two days later for a follow up visit at the antenatal clinic and no fetal heart rate was detectable.

Labor was induced two days after fetal demise was detected and a male fetus was delivered weighing 1940 grams, on the 10th centile for birth weight and a placental weight of 372g. It was noted there was thick meconium staining of amniotic fluid. Autopsy reported a grossly externally macerated fetus of normal morphology with weights and measurements consistent with 35 weeks gestation. There was marked maceration of the internal organs and overlapping of the skull bones.

There were no signs of infection or placental insufficiency. The report did not attribute a cause of death or an estimated date of demise.

Comment

Asthma is recognized as a risk factor during pregnancy [9-11]. There are a number of reports that show there is an increased risk of stillbirth in asthmatic pregnancies [9,12-15]. Fetal demise in pregnancies associated with asthma are thought to be caused by the development of maternal alkalosis [14] and reductions in fetal oxygenation resulting in fetal hypoxia, hypercapnia and acidosis [16].

The fetal death in this case appears to be related to the effects of a severe exacerbation and uncontrolled asthma during pregnancy. The woman had a history of moderately severe asthma with numerous admissions to hospital but had not used ICS for 2 years due to improved symptoms however there is evidence from the case record that she was experiencing asthma symptoms from early pregnancy and yet she received only reliever therapy without the necessary ICS. The fetus was small for gestational age supporting that there was growth restriction due to uncontrolled asthma during pregnancy [15,17]. On admission she was experiencing a severe exacerbation with a poor response to salbutamol and received suboptimal treatment. The recommended treatment for an adult with acute asthma is currently three nebulizations over one hour with supplemental oxygen if hypoxia is present [18] in addition to systemic steroid which she did receive. The combination of growth restriction and maternal hypoxia would likely have had an adverse effect on the fetus. The death of the fetus, although not reported in the autopsy is likely to have occurred days prior to its discovery [19,20] towards the end of admission or within hours after discharge as the ultrasound performed early in her admission showed a live fetus. Fetal movement and a fetal heart rate were last documented the day after the scan, 3 days before her discharge. Nursing notes mention "attention to fetal heart" on the day of discharge yet no heart rate was documented.

The circumstances leading to this death highlight the need for close management of asthma during pregnancy with a focus on specialist respiratory care which includes providing the asthma patient with education in control, management and a crisis plan for pregnancy [21,22].

Asthma exacerbations are of considerable concern during pregnancy due to the adverse effect they have on the fetus [23]. Schatz et al. found that of 1739 women with asthma, 20% had a severe exacerbation during pregnancy which required medical intervention. Exacerbations increased with increasing asthma severity, with 52% of severe asthmatics having an exacerbation.

Exacerbations can occur at any time during gestation but tend to cluster between 17 and 34 weeks gestation with a median of 25 weeks gestation [2]. Previous studies report similar results [24]. This suggests that the most important time to focus on asthma control and maternal self-management skills is early in gestation with continued follow up throughout pregnancy.

Inhaled steroid use for the treatment of asthma during pregnancy significantly reduces the incidence of acute exacerbations during gestation [17,25,26], decreases the number of hospital admissions [27] and reduces the need for regular use of oral steroid which is associated with low birthweight [25,28]. Stenius-Aarniala et al. [25] concluded that when asthmatic women were carefully managed by both obstetricians and respiratory physicians the rate of preterm delivery, perinatal death and low birth weight was not significantly different from the non-asthmatic population. Our previous studies are also in agreement with these findings [21,22,29].

It is impossible to identify a single etiology for stillbirth as there are many potential factors that contribute to a poor outcome for the fetus. In this particular case, the combination of a low birth weight fetus, male sex [30], a primigravid pregnancy and low socioeconomic status [31] could also have contributed to this poor outcome. However this case study highlights that the presence of chronic maternal asthma, an acute asthma exacerbation and a male fetus

further increases the possibility of a perinatal death, especially when exacerbations occur in late gestation when fetal demand for oxygen and nutrients has increased. The use of preventative clinical practices that include asthma education and management in the antenatal setting may reduce the risk of stillbirth in pregnancies complicated by asthma [22].

Condensation

This paper is an examination of a stillbirth in a pregnancy complicated by asthma.

Funding

National Health and Medical Research Council of Australia (Grant No. 252438), The Asthma Foundation of NSW, the NSW Department of Health and Hunter Medical Research Institute. A/Prof Vicki Clifton was a recipient of National Health and Medical Research Council RD Wright Fellowship during the collection of this data (Grant No. 300786). VC salary is currently funded by the National Health and Medical Research Council Senior Research Fellowship (APP1041918).

References

- Dombrowski MP, Schatz M, Wise R, Momirova V, Landon M, et al. (2004) Asthma during pregnancy. *Obstet Gynecol* 103: 5-12.
- Murphy VE, Gibson P, Talbot PI, Clifton VL (2005) Severe asthma exacerbations during pregnancy. *Obstet Gynecol* 106: 1046-1054.
- Hodyl NA, Stark MJ, Scheil W, Grzeskowiak LE, Clifton VL (2014) Perinatal outcomes following maternal asthma and cigarette smoking during pregnancy. *Eur Respir J* 43: 704-716.
- Clifton VL, Engel P, Smith R, Gibson P, Brinsmead M, et al. (2009) Maternal and neonatal outcomes of pregnancies complicated by asthma in an Australian population. *Aust N Z J Obstet Gynaecol* 49: 619-626.
- Clifton VL, Giles WB, Smith R, Bisits AT, Hempenstall PA, et al. (2001) Alterations of placental vascular function in asthmatic pregnancies. *Am J Respir Crit Care Med* 164: 546-553.
- Campaign National Asthma. *Asthma Management Handbook*. Sydney, Australia.
- Health NIO. *Guidelines for the diagnosis and management of asthma*. National Heart, Lung and Blood Institute.
- Barnes NC, Marone G, Di Maria GU, Visser S, Utama I, et al. (1993) A comparison of fluticasone propionate, 1 mg daily, with beclomethasone dipropionate, 2 mg daily, in the treatment of severe asthma. International Study Group. *Eur Respir J* 6: 877-885.
- Gelber M, Sidi Y, Gassner S, Ovadia Y, Spitzer S, et al. (1984) Uncontrollable life-threatening status asthmaticus--an indicator for termination of pregnancy by cesarean section. *Respiration* 46: 320-322.
- Gilchrist DM, Friedman JM, Werker D (1991) Life-threatening status asthmaticus at 12.5 weeks' gestation. Report of a normal pregnancy outcome. *Chest* 100: 285-286.
- Raphael JH, Bexton MD (1993) Combined high frequency ventilation in the management of respiratory failure in late pregnancy. *Anaesthesia* 48: 596-598.
- Gordon M, Niswander KR, Berendes H, Kantor AG (1970) Fetal morbidity following potentially anoxigenic obstetric conditions. VII. Bronchial asthma. *Am J Obstet Gynecol* 106: 421-429.
- Bahna SL, Bjerkedal T (1972) The course and outcome of pregnancy in women with bronchial asthma. *Acta Allergol* 27: 397-406.
- Sachs BP, Brown RS, Yeh J, Acker D, Niaraki M (1987) Is maternal alkalosis harmful to the fetus? *Int J Gynaecol Obstet* 25: 65-68.
- Greenberger PA, Patterson R (1988) The outcome of pregnancy complicated by severe asthma. *Allergy Proc* 9: 539-543.
- Cousins L (1999) Fetal oxygenation, assessment of fetal well-being, and obstetric management of the pregnant patient with asthma. *J Allergy Clin Immunol* 103: S343-349.
- Fitzsimons R, Greenberger PA, Patterson R (1986) Outcome of pregnancy in women requiring corticosteroids for severe asthma. *J Allergy Clin Immunol* 78: 349-353.
- Australia. NAC. *Australian Asthma Handbook Version 1.0: National Asthma Council Australia, Melbourne Website*. [http://www.asthmahandbook.org.au, 2014].
- Genest DR, Singer DB (1992) Estimating the time of death in stillborn fetuses: III. External fetal examination; a study of 86 stillborns. *Obstet Gynecol* 80: 593-600.
- Langley FA (1971) The perinatal postmortem examination. *J Clin Pathol* 24: 159-169.
- Murphy VE, Gibson PG, Talbot PI, Kessell CG, Clifton VL (2005) Asthma self-management skills and the use of asthma education during pregnancy. *Eur Respir J* 26: 435-441.
- Powell H, Murphy VE, Taylor DR, Hensley MJ, McCaffery K, et al. (2011) Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial. *Lancet* 378: 983-990.
- Murphy VE, Clifton VL, Gibson PG (2006) Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. *Thorax* 61: 169-176.
- Gluck JC, Gluck P (1976) The effects of pregnancy on asthma: a prospective study. *Ann Allergy* 37: 164-168.
- Stenius-Aarniala B, Piiirilä P, Teramo K (1988) Asthma and pregnancy: a prospective study of 198 pregnancies. *Thorax* 43: 12-18.
- Murphy VE, Gibson PG, Smith R, Clifton VL (2005) Asthma during pregnancy: mechanisms and treatment implications. *Eur Respir J* 25: 731-750.
- Wendel PJ, Ramin SM, Barnett-Hamm C, Rowe TF, Cunningham FG (1996) Asthma treatment in pregnancy: a randomized controlled study. *Am J Obstet Gynecol* 175: 150-154.
- Perlow JH, Montgomery D, Morgan MA, Towers CV, Porto M (1992) Severity of asthma and perinatal outcome. *Am J Obstet Gynecol* 167: 963-967.
- Murphy VE, Gibson PG, Giles WB, Zakar T, Smith R, et al. (2003) Maternal asthma is associated with reduced female fetal growth. *Am J Respir Crit Care Med* 168: 1317-1323.
- Engel PJ, Smith R, Brinsmead MW, Bowe SJ, Clifton VL (2008) Male sex and pre-existing diabetes are independent risk factors for stillbirth. *Aust N Z J Obstet Gynaecol* 48: 375-383.
- Goy J, Dodds L, Rosenberg MW, King WD (2008) Health-risk behaviours: examining social disparities in the occurrence of stillbirth. *Paediatr Perinat Epidemiol* 22: 314-320.