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ORIGINAL ARTICLE

A prospective cohort study of pulmonary function during pregnancy in women with and without asthma

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Abstract

Background and objective: Pregnancy alters the severity of asthma unpredictably. Uncertainty still exists about longitudinal changes in pulmonary function during pregnancy in both healthy and asthmatic women. This study aimed to compare pulmonary function changes during pregnancy in healthy and asthmatic women and to determine the relationship between pulmonary function and asthma-related quality of life during pregnancy. A secondary aim was to investigate the application of forced expiratory volume in 6 s (FEV₆) for monitoring asthma during pregnancy. **Methods:** Pregnant women with ($n = 20$) and without asthma ($n = 20$) had pulmonary function tests at 8–20, 21–28 and 29–40 weeks gestation. Those with asthma also completed the Asthma Control Questionnaire (ACQ) and mini Asthma Quality of Life Questionnaire (mAQLQ) at each visit. **Results:** Pulmonary function declined in both groups at follow-up #1 (more markedly in those with asthma) but then improved at follow-up #2 (more markedly in those with asthma). In those with asthma, ACQ scores increased, while mAQLQ scores declined at follow-up #1; whilst at follow-up #2 these changes were in the opposite direction. FEV₆ and forced vital capacity (FVC) were highly correlated ($r = 0.88, p < 0.01$) in asthmatics. **Conclusions:** Pulmonary function changes during second and third trimesters were more pronounced in asthmatics than in healthy women. FEV₆ monitoring may assist pregnant women and their health professionals in optimizing asthma management. The changes in pulmonary function in women with asthma were not significantly associated with changes in asthma control or asthma-related quality of life.

Keywords

Asthma, pregnancy, pulmonary function, spirometry

History

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Introduction

Uncertainty still exists about the longitudinal changes in pulmonary function during pregnancy in both healthy women and those with asthma. During pregnancy asthma improves in nearly a third of patients, worsens in slightly more than one-third, and remains unchanged in one-third [1]. Some pregnant women with asthma may have few symptoms, but their pulmonary function may be abnormal, putting the health of mother and fetus at risk [2]. Since pregnancy alters the severity of asthma unpredictably, patients should be monitored closely so that any changes in asthma control can be matched with appropriate changes in management. Regular objective monitoring in conjunction with assessment of asthma-related quality of life (QoL) and asthma control

might help early detection of worsening asthma by patients and health professionals, enabling changes in management.

Spirometry is still the best means of monitoring and assessing asthma severity [3]. For pregnant women with asthma, spirometry should be conducted early in pregnancy and periodically, as needed [4]. Forced expiratory volume in 6 s (FEV₆) has been shown to be equivalent to forced vital capacity (FVC) in consecutive patients referred to a New Zealand tertiary hospital respiratory laboratory for spirometry [5]. Performing FEV₆ is easier, more achievable, more reproducible and less physically demanding than FVC [5–7]. FEV₆ has the advantage that at the end of a spirometry measurement, the result is more explicitly defined and easier to achieve compared to FVC [8]. However, FEV₆ has not been used in prospective evaluation of lung function during pregnancy.

This study aimed to: (i) compare changes in pulmonary function during pregnancy between healthy women and those with asthma; (ii) determine the relationship between changes

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in pulmonary function and asthma-related QoL in pregnancy and (iii) investigate the application of FEV₆ in monitoring asthma during pregnancy.

Methods

Subjects

Pregnant women with a singleton pregnancy aged ≥ 18 years and able to communicate in English were recruited when attending scheduled antenatal visits at the Mercy Hospital for Women, Melbourne, Australia. The healthy group had no history of asthma and none of the participants in either group had a history of hypertension or cardiovascular disease. Pregnant women who self-reported asthma at the time of booking their first antenatal clinic visit and had used any asthma medication (anti-inflammatory or bronchodilator) during or in the 12 months before the current pregnancy were eligible for inclusion. The study was approved by the Human Research Ethics Committees of Monash University and the Mercy Hospital for Women. Written informed consent was obtained from all participants.

Design

A prospective cohort study was conducted to observe changes in pulmonary function. Pulmonary function (pre-bronchodilator) was measured, seated; three times (gestational weeks 8–20, 21–28, and 29–40) in the Respiratory Laboratory, Austin Health, using a spirometer (Jaeger MasterScreen, Carefusion, Hoerschberg, Germany). All spirometry variables were reported to American Thoracic Society/European Respiratory Society (ATS/ERS) 2005 standards [9]. Spirometry was not performed if participants self-reported respiratory infection at a particular visit to avoid compromising the quality of the maneuver due to coughing or sneezing and to reduce infection control hazards.

Study outcomes

Pulmonary function parameters measured or calculated at the three time points included FEV₁, FEV₆, FVC, FEV₁/FEV₆ and FEV₁/FVC. FEV₁ and FVC were also expressed as percentage (%) predicted values using the National Health and Nutrition Examination Survey (NHANES III) reference equations. A standard ethnicity correction 0.88 for non-Caucasian subjects was applied as suggested by ATS/ERS 2005 guidelines [10].

Asthma control and asthma-related QoL were assessed prior to spirometry using the Asthma Control Questionnaire (ACQ) 7 questions [11] and mini Asthma Quality of Life Questionnaire (mAQLQ) [12], respectively. An ACQ score of ≥ 1.5 suggested that asthma was not well controlled; and a change in ACQ score by ≥ 0.5 was regarded as clinically significant [minimum clinically important difference (MCID)] [13]. The mAQLQ measures the functional (physical, emotional, occupational and social) problems that concerned patients with asthma. The maximum score on mAQLQ was 7, which meant there was no impairment due to asthma [12].

Neonatal characteristics including Activity Pulse Grimace Appearance Respiration (APGAR) scores at 1 and 5 min,

gestational age, birth weight, length and head circumference were recorded at delivery. Birth weight centiles were calculated using www.gestation.net/grow-au.aspx, which adjusted for maternal characteristics including height, weight, ethnicity, parity and fetal gender.

Statistical analysis

Statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary, NC) and SPSS version 19.0 (IBM SPSS Statistics for Windows, Armonk, NY). Differences in demographic characteristics, and maternal and fetal outcomes were examined using χ^2 tests, unpaired *t*-tests or Mann–Whitney *U*-tests where appropriate. Univariate correlations were determined using Pearson's *r* and Spearman's ρ . All reported *p* values were two-sided and not adjusted for multiple comparisons. A *p* < 0.05 indicated statistical significance.

Pulmonary function parameters were the main outcome measures. A longitudinal analysis was performed using the PROC MIXED procedure in SAS with patients treated as random effects. Models were fitted using main effects for group (asthma versus healthy), time (baseline, follow-up visits #1 and #2) and an interaction between group and time to ascertain if the groups behaved differently over time. To account for any baseline imbalances, baseline values of outcomes were included as potential covariates in these models. The PROC MIXED procedure uses a restricted maximum likelihood algorithm that enables specific modeling of the within-patient covariance structure. Using an Akaike information criterion (AIC) to determine goodness of fit, an auto regressive (order 1) covariance structure was found to produce the best fit to data. All observed data were considered for analysis, with the mixed-effects models treating missing values as being missing at random. *Post hoc* pairwise comparisons were performed to assess between group differences at follow-up visits and within group differences between follow-up visits.

Results

The flow of participants through the study is illustrated in Figure 1. Forty pregnant women (20 healthy, 20 with asthma) were recruited between 11 and 19 weeks of gestation. All participants completed baseline spirometry including FEV₆ measurement prior to 20 weeks gestation. The characteristics of the sample are summarized in Table 1. There were no significant differences in demographic or maternal characteristics between women with and without asthma. Twelve (60%) women with asthma used short-acting beta agonists (SABA) as needed only, while the rest also used an inhaled corticosteroid (ICS) or an ICS long-acting beta agonist (LABA) combination. None of the women with asthma self-reported any comorbidities.

Changes in pulmonary function

When the pulmonary function parameters were analyzed with the mixed-effects models, significant group $\times$ time interaction effects were found for FEV₁ (*p* = 0.04), FEV₁% predicted (*p* = 0.042) and FEV₁/FVC% predicted (*p* = 0.01). Changes in pulmonary function during pregnancy were similar in both

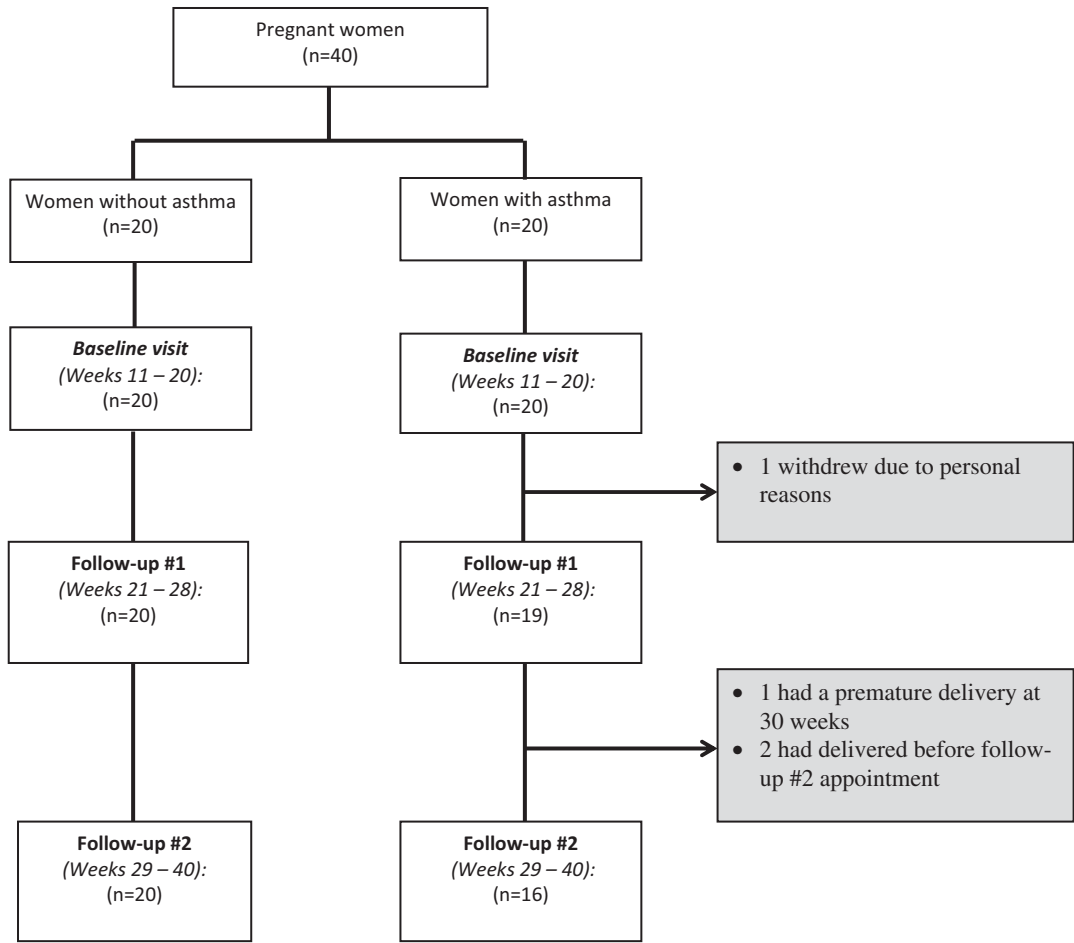


Figure 1. Flow of study subjects through the study.

groups. At baseline, there were no statistically significant differences in pulmonary function between groups (Table 2). At follow-up #1, pulmonary function declined in both groups, but women with asthma had a greater reduction. At follow-up #2, both groups showed improvement in pulmonary function compared to follow-up #1. FEV₁, FEV₁% predicted (both $p = 0.02$) and FEV₁/FVC% predicted ($p = 0.01$) values were significantly different between healthy and asthmatic groups at follow-up #2. These changes are also illustrated in Figure 2.

The within group differences in FEV₁, FEV₆, FVC, FEV₁% and FEV₁/FVC% predicted at the first and second follow-ups compared to baseline are presented in Table 3. In the healthy group, mean baseline FEV₁ dropped by 101 and 43 ml at follow-ups #1 and #2, respectively. On the other hand, women with asthma had a mean reduction in baseline FEV₁ of 139 ml at follow-up #1, which subsequently increased by 51 ml to higher than baseline levels at follow-up #2.

Changes in ACQ and mAQLQ

In women with asthma, the decline in pulmonary function at follow-up #1 was also marked by a reduction in asthma control (i.e. increase in ACQ score) and QoL (i.e. decline in mAQLQ score). At follow-up #2 these changes were in the opposite direction, suggesting improvement in

pulmonary function, better asthma control and QoL (Figure 3). At follow-up #1 ACQ score increased >0.5 (MCID) in 58% of the asthmatic group, decreased in 21%, and remained unchanged in 21%. At follow-up #2 ACQ score increased in 19%, decreased in 56% and remained unchanged in 25%. A strong inverse correlation was found between ACQ and mAQLQ at follow-ups #1 ($r = -0.74$; $p < 0.01$) and #2 ($r = -0.75$; $p < 0.01$). However, correlations between pulmonary function parameters and both ACQ and mAQLQ were very weak.

Correlations between FEV₆ and FVC

At follow-up #1, compared to non-asthmatics, women with asthma had a greater decline in FEV₆ and the decrease of FEV₆ in the asthmatic group was also followed by the reduction in FVC (Table 3). However, at follow-up #2 the differences in reductions of FEV₆ and FVC from baseline between the groups were not significant. There were strong, positive correlations between changes in FEV₆ and FVC from baseline to follow-up #1 ($r = 0.88$, $p < 0.01$) and from follow-up #1 to follow-up #2 ($r = 0.85$, $p < 0.01$).

Maternal and neonatal characteristics

Pregnant women with asthma delivered slightly shorter babies ($p = 0.02$) with lower APGAR scores at one minute ($p = 0.01$) compared to those without asthma (Table 1). Nevertheless,

Table 1. Demographic, maternal and neonatal characteristics of the study participants.

	Without asthma (n = 20)	With asthma (n = 20)	p Value
Demographic characteristics	n (%)	n (%)	
Race			0.34
Caucasian	16 (80)	19 (95)	
Asian	4 (20)	1 (5)	
Past smoker	8 (40)	6 (30)	0.51
Gravidity			0.74
Primigravid	6 (30)	7 (35)	
Multigravid	14 (70)	13 (65)	
Maternal characteristics	Mean ± SD	Mean ± SD	
Age (year)	33.2 ± 5.0	32.3 ± 3.1	0.47
Height (cm)	165.8 ± 6.7	162.1 ± 6.6	0.08
BMI (kg/m ²) at baseline*	24.7 (21.9–27.0)	26.1 (22.7–30.5)	0.30
Weight (kg) at			
Baseline	70.7 ± 15.8	74.2 ± 20.0	0.56
Follow-up #1	72.9 ± 14.7	78.3 ± 19.5	0.34
Follow-up #2	79.5 ± 15.0	80.9 ± 19.1	0.79
Gestational age (weeks) at*			
Baseline	16 (16–17)	15.5 (13.3–17)	0.28
Follow-up #1	24 (22–26)	25.5 (24–27)	0.15
Follow-up #2	35 (34–36)	35.5 (34.3–36.8)	0.65
Duration of asthma (years)*	–	24.5 (18.5–29.8)	–
Asthma severity	–		–
Intermittent to mild		12 (60%)	–
Moderate to severe		8 (40%)	–
Asthma medications			
SABA only	–	12 (60%)	–
ICS + SABA	–	1 (5%)	–
ICS/LABA + SABA	–	7 (35%)	–
Neonatal characteristics	Median (interquartile range)	Median (interquartile range)	
Gestational age	39.9 (38.6–40.5)	39.4 (39–40.7)	1
Mode of delivery [n (%)]			
Vaginal delivery	16 (80)	11 (55)	0.09
Emergency cesarean	2 (10)	5 (25)	0.41
Elective cesarean	2 (10)	2 (10)	1.00
Forceps/vacuum	0 (0)	2 (10)	0.48
Birth weight (gm)	3600 (3339–3745)	3400 (3118–3523)	0.13
Birth weight percentile <10th [n (%)]	2 (10%)	2 (10%)	1.00
Birth length (cm)	51.5 (51–52)	50.3 (47.4–51)	0.02
Head circumference (cm)	34.5 (34.4–36)	34.25 (33.6–35)	0.33
APGAR scores at 1 min	9 (9–9)	9 (6.25–9)	0.01
APGAR scores at 5 min	9 (9–9.75)	9 (9–9)	0.24

*Median (interquartile range).

Table 2. Pulmonary function parameters during pregnancy in women with and without asthma.

Test	Baseline		Follow-up #1		Follow-up #2	
	Without asthma n = 20	With asthma n = 20	Without asthma n = 20	With asthma n = 19	Without asthma n = 20	With asthma n = 16
FEV ₁ (L)	3.18 ± 0.03	3.17 ± 0.03	3.08 ± 0.03	3.04 ± 0.03	3.14 ± 0.03	3.24 ± 0.03*
FEV ₆ (L)	3.87 ± 0.03	3.87 ± 0.03	3.80 ± 0.03	3.71 ± 0.03	3.83 ± 0.03	3.85 ± 0.03
FVC (L)	3.91 ± 0.03	3.90 ± 0.03	3.85 ± 0.03	3.77 ± 0.04	3.87 ± 0.03	3.86 ± 0.03
FEV ₁ %	100.37 ± 0.90	100.00 ± 0.90	96.92 ± 0.90	95.75 ± 0.92	99.07 ± 0.90	102.13 ± 0.99*
FVC %	103.20 ± 0.86	103.14 ± 0.86	101.25 ± 0.86	99.41 ± 0.88	102.35 ± 0.86	102.15 ± 0.96
FEV ₁ /FVC	81.97 ± 0.84	81.12 ± 0.84	80.47 ± 0.84	81.72 ± 0.84	80.92 ± 0.84	83.80 ± 0.93
FEV ₁ /FVC% predicted	97.37 ± 0.70	96.19 ± 0.73	95.57 ± 0.70	94.36 ± 0.72	96.12 ± 0.70	98.71 ± 0.78*
FEV ₁ /FEV ₆	82.53 ± 0.55	81.65 ± 0.55	81.42 ± 0.55	81.16 ± 0.57	82.41 ± 0.55	83.69 ± 0.61
ACQ score	–	0.5 (0.3–1.2)	–	1.43 (1–1.6)	–	0.7 (0.4–1.4)
mAQLQ score	–	6.1 (5.6–6.5)	–	5.3 (4.9–6.2)	–	6.2 (5.3–6.6)

FEV₁%, FEV₁ expressed as a percentage of the predicted value; FVC%, FVC expressed as a percentage of the predicted value. Pulmonary function data are presented as mean ± SE; ACQ and mAQLQ scores as median (interquartile range).

Significantly different from healthy **p* < 0.05.

there were no differences noted in 5 min APGAR or customized birth weight centile which are better measures of acute and chronic fetal compromise due to placental insufficiency, respectively. Two women in the asthma group

reported symptoms in Weeks 21–28 and were prescribed prednisolone 50 mg daily for 2 weeks; one of them presented to the emergency department due to asthma exacerbation and was hospitalized. Only 55% women in the asthma group had a

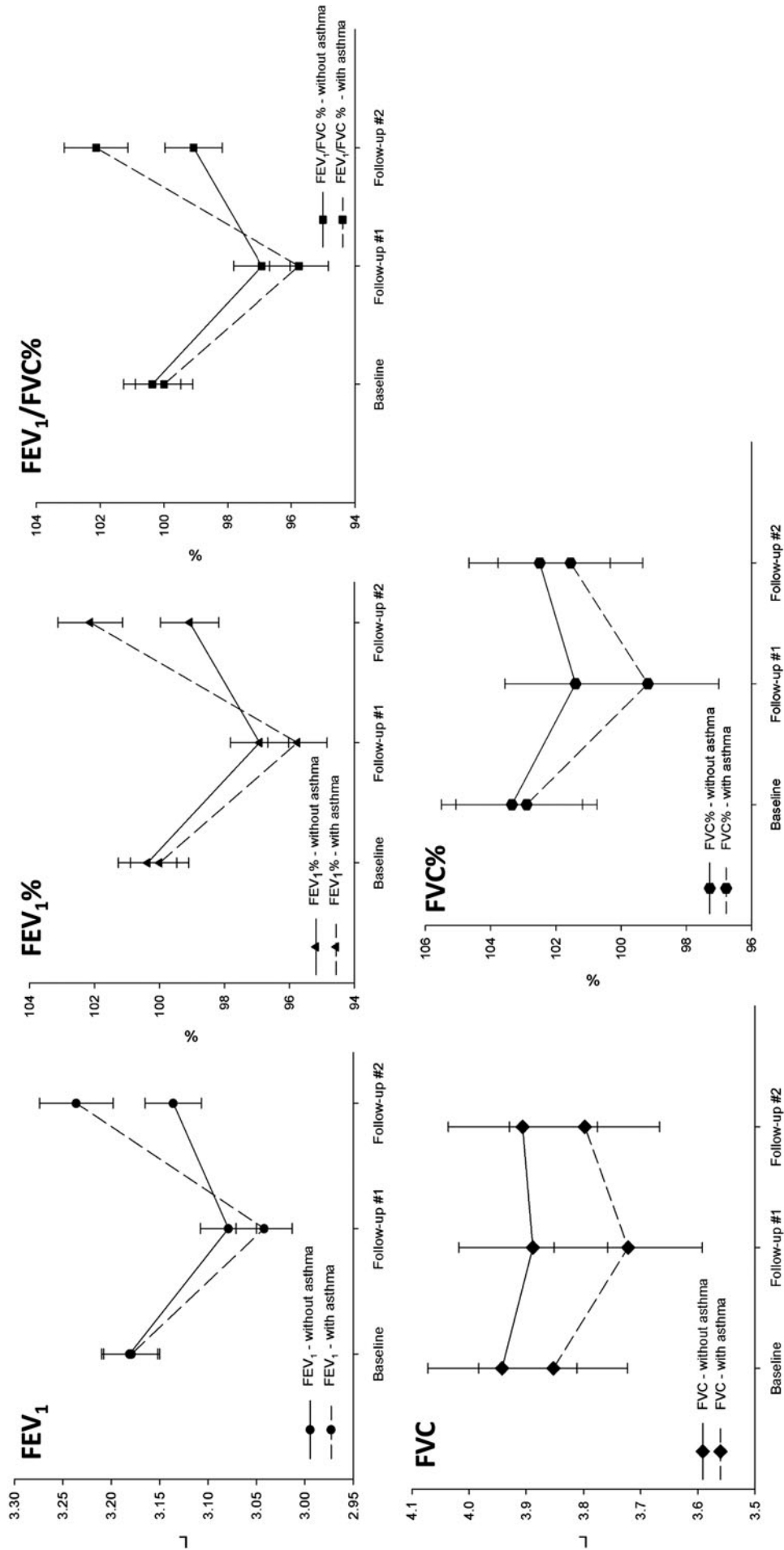


Figure 2. FEV₁, FVC, FEV₁%, FVC% and FEV₁/FVC during pregnancy in women with and without asthma. Data are expressed as mean ± SE.

Table 3. Changes from baseline in pulmonary function, asthma control score and asthma-related QoL in women with and without asthma.

Test	Mean difference (95% CI)			
	Without asthma		With asthma	
	Follow-up #1	Follow-up #2	Follow-up #1	Follow-up #2
FEV ₁ (ml)	101 (29,172)	43 (–28,115)	139 (65,212)	–51 (–130, 28)
FEV ₆ (ml)	71 (–5,147)	47 (–29,123)	159 (8, 237)	46 (–37,129)
FVC (ml)	52 (–34,138)	34 (–52,121)	134 (45, 222)	58 (–36, 153)
FEV ₁ %	3.20 (0.98,5.41)	1.05 (–1.17, 3.26)	4.55 (2.27, 6.83)	–1.73 (–4.20, 0.74)
FVC%	1.92 (–0.14, 3.98)	0.82 (–1.24, 2.88)	3.74 (1.63, 5.86)	1.35 (–0.92, 3.62)
FEV ₁ /FVC	0.92 (–1.11, 2.95)	0.47 (–1.56, 2.50)	0.12 (–1.93, 2.17)	–2.05 (–4.31, 0.21)
FEV ₁ /FVC% predicted	1.02 (–0.65, 2.69)	0.47 (–1.20, 2.14)	2.88 (1.14, 4.62)	–1.56 (–3.41, 0.29)
FEV ₁ /FEV ₆	0.51 (–0.78, 1.79)	–0.49 (–1.77, 0.79)	1.25 (–0.08, 2.58)	–1.37 (–2.80, 0.05)
ACQ scores	–	–	–0.36 (–0.44, 0.30)	–0.14 (–0.65, 0.56)
mAQLQ scores	–	–	0.29 (–0.32, 0.43)	0.02 (–0.69, 0.71)

FEV₁%, FEV₁ expressed as a percentage of the predicted value; FVC%, FVC expressed as a percentage of the predicted value. There were no significant differences between the groups at baseline. Values represent mean difference (CI) compared with baseline. Positive means values lower than baseline (decrease) and negative means values higher than baseline (increase).

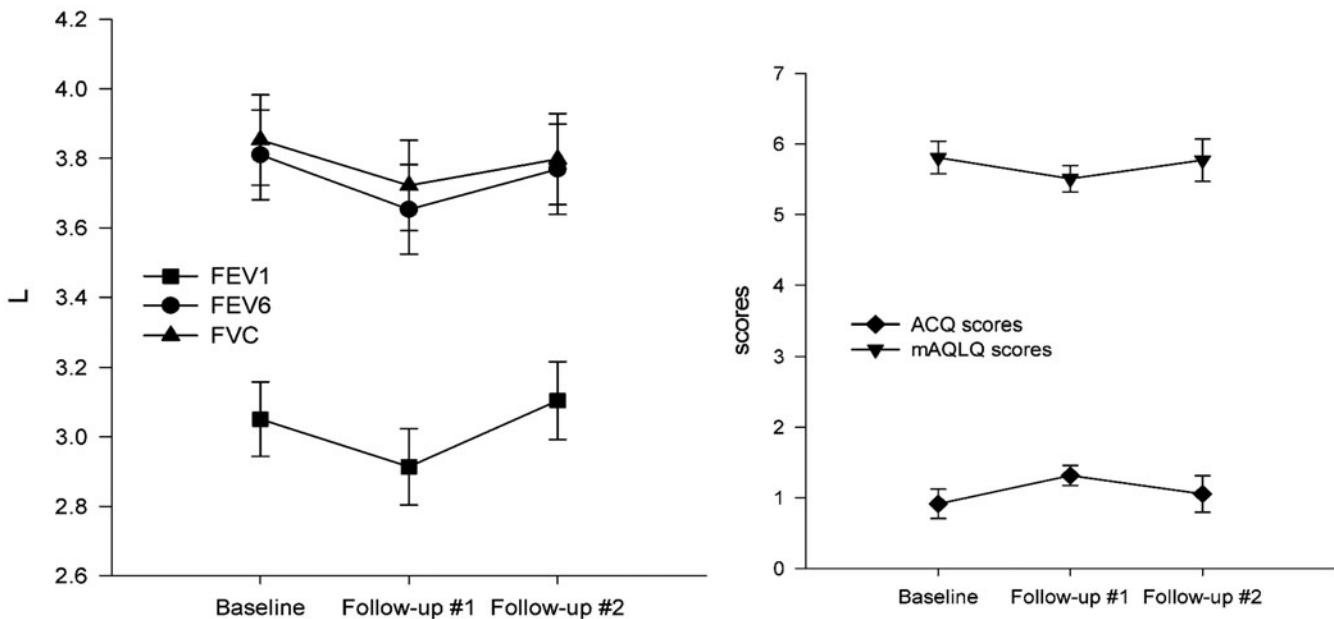


Figure 3. Pulmonary parameters, ACQ and mAQLQ scores in women with asthma.

normal vaginal delivery compared to 80% in those without asthma ($p = 0.09$).

Discussion

Changes in spirometry during pregnancy differed significantly between women with and without asthma. Compared to their counterparts, women with asthma showed a greater reduction of FEV₁ from baseline at follow-up #1, but had better pulmonary function at follow-up #2, the latter result being consistent with a previously described reduction in bronchial hyper responsiveness later in pregnancy [14]. The majority of the asthmatic group (60%) had mild asthma, as reflected by their use of only occasional SABA and the overall well preserved interval lung function, as is

commonly seen in people with intermittent or mild persistent asthma [15].

Shortness of breath, often referred to as “physiologic dyspnea”, is a common symptom during pregnancy [16]. Physical examination and spirometry can be used to distinguish physiologic dyspnea from pathologic dyspnea [17]. Physiologic dyspnea often occurs while at rest or with mild exertion; but when accompanied by other symptoms such as wheezing or cough is possibly due to asthma [17]. White et al [18] showed that some women with infrequent-mild asthma felt subjectively better during pregnancy when they were asked to self-report symptoms using diary cards, although no improvements were found in pulmonary function. Ideally, monitoring asthma changes during pregnancy should not rely on subjective patient perceptions alone; spirometry and

Table 4 Summary of pulmonary function parameters in our study and previous studies during pregnancy.

Tests	Our findings*		Sims [24]		Grindheim [20]	Nørregard [21]	Puranik [22]	Siddiqui [23]
	Without asthma n = 20	With asthma n = 20	Without asthma n = 12	With asthma n = 27	Without asthma n = 100	Without asthma n = 39	Without asthma n = 50	Without asthma n = 60
Gestational age: 8–20 weeks								
FEV ₁ (L)	3.18 ± 0.03	3.17 ± 0.03	–	–	3.18 ± 0.44	–	2.00 ± 0.09	–
FVC (L)	3.91 ± 0.03	3.90 ± 0.03	–	–	3.89 ± 0.48	–	2.19 ± 0.25	–
FEV ₁ %	100.37 ± 0.90	100.00 ± 0.90	–	–	98.2 ± 11.10	104.0 ± 12.00	–	–
FVC%	103.20 ± 0.86	103.14 ± 0.86	99.3 ± 12.20	96.90 ± 9.50	–	–	–	–
FEV ₁ /FVC	81.97 ± 0.84	81.12 ± 0.84	81.40 ± 4.40	83.30 ± 6.10	–	–	–	–
FEV ₁ /FVC%	97.37 ± 0.70	96.19 ± 0.73	–	–	–	–	92.60 ± 5.01	–
Gestational age: 21–28 weeks								
FEV ₁ (L)	3.08 ± 0.03	3.04 ± 0.03	–	–	3.16 ± 0.39	–	2.07 ± 0.25	–
FVC (L)	3.85 ± 0.03	3.77 ± 0.04	–	–	3.96 ± 0.51	–	2.10 ± 0.28	–
FEV ₁ %	96.92 ± 0.90	95.75 ± 0.92	–	–	99.1 ± 11.40	96.0 ± 12.00	–	–
FVC%	101.25 ± 0.86	99.41 ± 0.88	101.20 ± 12.10	82.60 ± 6.80	–	–	–	–
FEV ₁ /FVC	80.47 ± 0.84	81.72 ± 0.84	83.40 ± 4.40	82.60 ± 6.80	–	–	–	–
FEV ₁ /FVC%	95.57 ± 0.70	94.36 ± 0.72	–	–	–	–	98.63 ± 3.54	–
Gestational age: 29–40 weeks								
FEV ₁ (L)	3.14 ± 0.03	3.24 ± 0.03	–	–	3.21 ± 0.43	–	2.15 ± 0.21	2.17 ± 0.25
FVC (L)	3.87 ± 0.03	3.86 ± 0.03	–	–	4.00 ± 0.53	–	2.21 ± 0.27	2.47 ± 0.29
FEV ₁ %	99.07 ± 0.90	102.13 ± 0.99	–	–	99.3 ± 11.30	96.0 ± 19.00	–	88.64 ± 5.62
FVC%	102.35 ± 0.86	102.15 ± 0.96	102.20 ± 11.2	95.50 ± 13.10	–	–	–	86.48 ± 4.37
FEV ₁ /FVC	102.35 ± 0.86	102.15 ± 0.96	84.4 ± 3.5	82.80 ± 3.10	–	–	–	85.52 ± 2.32
FEV ₁ /FVC%	96.12 ± 0.70	98.71 ± 0.78	–	–	–	–	97.51 ± 4.04	–

Values are mean ± SDs except for *mean ± SEs.

validated asthma questionnaires may identify clinically significant changes in asthma [14,18,19].

Previous studies

Previous studies have not observed consistent changes in pulmonary function during healthy pregnancy. Table 4 compares the pulmonary parameters in our study to previous studies. While our study showed that FEV₁ and FVC decreased significantly at Weeks 21–28 in healthy subjects, Grindheim et al. [20] did not find a change in FEV₁ but showed that FVC increased significantly after Week 23, which was maintained at 6 months post-partum. Norregaard et al. [21] showed that FEV₁ decreased slightly during second and third trimesters, but then increased postpartum. The study by Puranik et al. [22] found that FEV₁ and FVC remained unchanged throughout normal pregnancy. Siddiqui et al. [23] demonstrated that pulmonary function parameters were not significantly different between healthy singleton and twin pregnancies in the last trimester (36 weeks gestation); while the values were lower in healthy pregnant women (singleton or twin pregnancy) than in non-pregnant women.

Sims et al. [24] measured FVC and FEV₁ in 27 pregnant women with asthma and 11 healthy pregnant women. The groups were not matched except for age. The asthmatic group had lower values at all-time points compared to controls. This study was not able to show significant longitudinal changes in FEV₁ and FEV₁/FVC between pregnancy and the non-pregnant state [24]. It also showed no indication that FEV₁ or FEV₁/FVC were affected by pregnancy either during exercise or at rest [24].

Our study sample was different from previous studies. Grindheim et al. [20], Norregaard et al. [21] and Sims et al. [24] studied European populations, while Puranik et al. [22] and Siddiqui et al. [23] studied Indian populations.

The differences in subjects’ ethnicity, sample size, medication use, data analysis methods, spirometer and measurement position (e.g. standing, sitting or supine) may account for differing results.

FVC versus FEV₆

We confirmed that FEV₆ and FVC are significantly correlated in pregnancy. FEV₆ and FEV₁/FEV₆ have been widely studied as surrogates for FVC and FEV₁/FVC, respectively [7], but have not previously been applied prospectively to monitor asthma in pregnancy. FEV₆ can be used as a substitute for FVC and has been shown to be equivalent to FVC in adults with asthma [5]. Longitudinal changes in FEV₆ and FVC during pregnancy in the asthmatic group were in the expected direction with changes in asthma control and asthma-related QoL, further supporting the potential use of FEV₆ for monitoring asthma in pregnancy.

A descriptive cross-sectional study by Nwagha et al. [25] in 172 healthy women with varying gestational ages [40 non-pregnant and 132 pregnant comprising 30 (<14 weeks), 48 (14–27 weeks) and 54 (>27 weeks)] showed that FVC and FEV₆ values were lower while the FEV₁/FVC and FEV₁/FEV₆ were higher as pregnancy progressed. Our study has confirmed longitudinal changes in FVC and FEV₆ in both women with and without asthma at various stages of pregnancy.

Our participants represented women attending major Australian maternity hospitals [26,27]. Although this study is limited by a small sample size, it is still sufficient to describe the longitudinal changes of pulmonary function during pregnancy in healthy women and those with asthma as they relate to gestational age. Statistically significant changes in pulmonary function may be meaningful to researchers, but of little clinical importance to patients [10]. The small

changes in FEV₁ and FVC observed in women with asthma in this study were possibly the result of restriction rather than obstruction as FEV₁/FVC did not change, suggesting asthma was not the major contributor to the pattern of pulmonary function changes in this group. The majority of studies in both adults and children have found no significant correlation between objective measures such as FEV₁/peak expiratory flow (PEF) and clinical asthma symptoms [3].

We observed some significant differences in pulmonary function between groups; hormonal, metabolic and physiological changes during pregnancy may alter the mechanics of breathing and pulmonary function in pregnant women. Pulmonary function changes during pregnancy are mediated initially by hormonal changes and later by the enlarging uterus [28]. In healthy women, there is usually adequate maternal compensation for the increase in oxygen demands, with the increases in tidal volume leading to a significant fall in partial pressure of carbon dioxide (pCO₂) [28]. The process appears to be mediated by rising levels of progesterone and augmented by a decrease in residual volume [28]. Progesterone and cortisol may affect the respiratory center [29]. Progesterone levels rise progressively in the first trimester and remain elevated until delivery resulting in stimulation of the respiratory center and smooth muscle relaxation [30]. Cortisol also rises sharply throughout pregnancy potentially leading to increased pulmonary glucocorticosteroid receptor interactions and effects causing smooth muscle relaxation [1,30].

Asthma symptoms may improve or worsen during pregnancy; hence appropriate management should be tailored to changes in pulmonary function. Various factors may contribute to poor QoL in pregnant women with asthma. Asthma changes unpredictably during pregnancy, and asthma symptoms usually worsen during the second and third trimesters, especially the sixth month, with improvement in the last 4 weeks [1,31]. Women who have poorly controlled asthma from the beginning of the pregnancy are likely to have more asthma symptoms throughout pregnancy; therefore they should be treated with appropriate medications and monitored closely [31]. Concerns about medication safety during pregnancy may prompt women to stop taking their medication without consulting their healthcare professionals leading to worsening symptoms and QoL [27,32]. However, in this study we did not assess asthma medication adherence at each visit.

Asthma self-management programs for pregnant women, involving regular monitoring of FEV₁ and FEV₆ in conjunction with assessment of asthma symptoms, should be evaluated in larger prospective studies for their ability to optimize health outcomes in women with varying severities of asthma. Future studies may also benefit from including longitudinal markers of inflammatory change in serum and possibly in exhaled condensate given the changes present at follow-up #1. A larger study with groups matched for body mass index (BMI), age, height and gestational age with more severe cases of asthma may also be beneficial.

In summary, we have demonstrated that pulmonary function declined during second trimester, then improved in the final weeks of gestation in both groups, but larger changes were found in women with asthma. Although the changes in pulmonary function were statistically significant in the asthma

group, they were modest. The changes in pulmonary function in women with asthma were not significantly associated with changes in asthma control or QoL. FEV₆ can be substituted for FVC for monitoring during pregnancy. Regular monitoring of FEV₁ and FEV₆, along with assessment of symptoms and medication adherence, may assist pregnant women and their health professionals in optimizing asthma management.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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