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Longitudinal Changes in Lung Function during Pregnancy: The Impact of Asthma

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ABSTRACT

Background: Pregnancy produces physiological effects on the respiratory system; the interplay of gestation and maternal asthma remains poorly characterized. Characterizing longitudinal lung function in pregnant women with and without asthma provides a potential opportunity to examine respiratory adaptations and risks during pregnancy.

Objective: To investigate the effect of advancing gestation, and its interaction with asthma, on lung function of pregnant women.

Methodology: This prospective longitudinal cohort study took place in Multan, Pakistan, and recruited 460 pregnant women (230 with asthma and 230 as non-asthmatic controls). Women were recruited at 12–22 weeks of gestation and followed until the third trimester. Spirometry was undertaken at three standardized time points to evaluate forced vital capacity (FVC%), forced expiratory volume in 1 second (FEV1%), and FEV1/FVC ratio according to ATS/ERS guidelines.

Results: At baseline, the asthmatic women demonstrated significantly lower FEV1% compared to their non-asthmatic counterparts (88.9 ± 9.3 vs. 94.8 ± 8.7). On average, FVC% decreased through gestation in both groups, but it decreased to a greater degree in the history of asthma group (–0.12% per week, 95% CI –0.16 to –0.08) compared to the asthmatic group (–0.07% per week, 95% CI –0.11 to –0.03). FEV1% declined significantly for non-asthmatic women but remained unchanged for the asthmatic women during pregnancy.

Conclusion: Pregnancy has differential effects on lung function when examining asthma status. Non-asthmatic women have relatively greater restrictive changes, while asthmatic women see stable expiratory function and can expect a modest improvement in FEV1/FVC ratio.

Keywords: Pregnancy; Asthma; Lung Function; Gestation

Introduction

Pregnancy is characterized by significant physiological and hormonal changes that affect nearly all organ systems, including the respiratory system. Pregnancy leads to changes in thoracic anatomy, increased oxygen requirements, and alterations in smooth muscle tone due to hormonal effects, all contributing to changes in pulmonary mechanics throughout pregnancy. In healthy women, these physiologic changes can affect respiratory function, and the effect may be amplified in women with pre-existing respiratory disease such as asthma.[1,2]

Spirometry is widely used to assess lung function and is the gold standard in diagnosing and monitoring obstructive airway disease. The clinical meaning of spirometric indices for pregnancy, specifically for women with asthma, and their clinical course have not been adequately investigated.[3]

Asthma is one of the most common chronic conditions complicating pregnancy and has a global prevalence from 4-12%.[4] The course of asthma in pregnant women is variable: about one-third will have worsening symptoms, one-third will improved symptoms, and the remainder will have unchanged symptoms.[5] Poorly controlled asthma in pregnancy is thought to increase the risk of adverse maternal and perinatal outcomes, such as preeclampsia, prematurity, low birth weight, and intrauterine growth restriction.[6,7] The association of poorly controlled asthma and adverse effects highlights that lung function must be monitored throughout gestation to ensure sustained respiratory stability in the mother and to optimize fetal health.

Multiple studies have attempted to characterize the trajectory of pulmonary function in pregnancy with conflicting results. Some studies showed small but significant decreases in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) during late gestation, which the investigators attributed to extrapulmonary restriction secondary to the gravid uterus.[8] Other study suggest no change or even increases in some measures of spirometry across trimesters.[9] These differences almost certainly result from methodological issues such as having small sample sizes, inability to use longitudinal follow-up, and multiple different participant selection methods. It is also important to note that few reports have included comparisons of lung function trajectories between pregnant women with and without asthma; therefore, although we learned a lot about respiratory physiology, there remain many gaps in our understanding of how asthma interacts with pregnancy on the respiratory system.[10]

In resources-limited regions, such as South Asia, the number of pregnant women suffering from maternal morbidity is high. Determining patterns of lung function in pregnant women with asthma is particularly relevant for South Asian populations due to environmental exposures, the prevalence of biomass fuel use, and differences in baseline anthropometric measures as compared with Western cohorts, all, of which, can impact lung function. However, little data is available from this region. Moreover, spirometry is not generally used as a tool in the limited routine antenatal care that occurs in developing countries, even though it is an inexpensive and non-invasive tool, and would provide valuable data on maternal respiratory health.

The need for region-specific evidence is emphasized in the context of Pakistan, where the prevalence of asthma is increasing, as are the rates for maternal health indicators which are lagging globally. Although international studies demonstrate potential for modest declines in FVC% and FEV1% during pregnancy, we do not know if these general trends are representative in Pakistani women, particularly with asthma and likely differing access and management of the condition. A longitudinal analysis of lung function in the Pakistani context could contribute information for antenatal care, and provide guidance to clinicians by describing findings for spirometry assessments during pregnancy.

The evidence on lung function trajectories in pregnancy is limited and inconsistent, particularly in women with asthma, highlighting the need for regionally generated data. This study was conducted in Multan, to investigate the longitudinal changes in lung function across gestation in a large, well-defined cohort of pregnant women with and without asthma. This study adds to the knowledge base regarding lung function in pregnancy by comparing trends in spirometry in the two groups and facilitates a better understanding of the relationship between progressing gestation and asthma on pulmonary function, and the implications for respiratory monitoring and antenatal care.

Objective

To investigate the effect of advancing gestation, and its interaction with asthma, on lung function of pregnant women.

Methodology

This study was designed as a prospective longitudinal cohort study conducted in Department of Gynaecology, Multan Medical & Dental College, Multan between August 2022 and September 2023. Pregnant women were recruited during their second trimester and followed until delivery. Lung function was assessed serially at multiple time points across gestation to examine the effect of advancing pregnancy, and its interaction with asthma, on spirometric indices.

The sample size was estimated based on expected differences in FEV1% between asthmatic and non-asthmatic pregnant women from previous literature.[1,11] Assuming a mean difference of 5% in FEV1% with a standard deviation of 15, a power of 80%, and alpha of 0.05, the required sample size was calculated to be at least 210 participants per group. To account for potential dropouts and incomplete data, a total of 230 women were recruited in each group. So total of 460 pregnant women were enrolled in this study. For this study, the population included 230 women with physician-diagnosed asthma, and 230 controls matched by age and gestational age who did not have asthma.

This study included pregnant women with women of at least 18 years of age and pregnancy between 12 and 22 weeks. We recruited two groups of individuals. The first group included individuals whose physician diagnosed them with asthma and who had used medication for asthma or reported symptoms in the last year. The second group included individuals who had never been diagnosed with asthma or any other ongoing breathing condition. Several factors led to disqualification from the study. These factors included having a different chronic lung condition (e.g., COPD or cystic fibrosis), being pregnant with twins or more, having a heart condition or other very serious illness that would affect breathing, or being unable to successfully complete the breathing test.

The study protocol (126-04/MMDC/2022) was approved by the Institutional Review Board (IRB) of Multan Medical & Dental College Multan. Written informed consent was obtained from all participants prior to enrolled in the study. The confidentiality of participants was maintained, and all procedures adhered to the ethical principles of the Declaration of Helsinki.

At enrollment, baseline demographic and clinical data were obtained, including maternal age, gestational age, parity, body mass index (BMI), smoking status, and medical history. Anthropometric measurements were recorded using standard protocols, and BMI was categorized as underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥ 30.0 kg/m²).

Asthma-related data included history of exacerbations, medication use, and symptom frequency. Asthma control was assessed using the Asthma Control Questionnaire (ACQ-6), with a score <1.5 considered controlled and ≥ 1.5 considered uncontrolled.

Lung function was measured using a portable spirometer with a best practices approach based on the guidelines set forth by the American Thoracic Society and European Respiratory Society (ATS/ERS). Each participant was guided through the test by trained respiratory technicians. Each participant made at least three acceptable breathing maneuvers to ensure accuracy with the procedures. From each participant's acceptable maneuvers, the best values were recorded for defined measurements of lung function as follows: Forced Vital Capacity (FVC); Forced Expiratory Volume in one second (FEV1); percentages of predicted values; and FEV1/FVC.

To monitor changes over time during pregnancy, the same spirometric measures at 3-point in time, mid-second trimester (18-22 weeks), late-second trimester (26-28 weeks) and third trimester (34-36 weeks). The expected normal predicted values for each participant were calculated using the Global Lung Initiative (GLI-2012) reference equations derived from individual characteristics of age, height, and ethnicity.

The data were entered and analyzed by SPSS version 26.0 (IBM Corp, Armonk, NY, USA). Continuous variables were represented as a mean ± standard deviation (SD), while categorical variables were represented by frequencies and percentages. Independent sample t-tests were used to assess baseline differences between the asthmatic women and non-asthmatic women for continuous variables, and chi-square tests were used for categorical variables.

For longitudinal analyses, linear mixed-effects regression models were used to assess trends in FVC%, FEV1%, and FEV1/FVC% in relation to gestation. Gestational age was modeled as a continuous fixed effect, and an interaction term for asthma status was included to test if the trends differed by asthma status. Random intercepts were included for each participant level to accommodate the repeated measurement aspect of the outcome variables. Models were adjusted for potential confounding factors of maternal age, BMI, and smoking status. Statistical significance was set at $p < 0.05$.

Results

A total of 460 pregnant women enrolled in the study, 230 of whom had asthma and 230 who did not. The mean age of the entire sample involved in the study was 27.6 ± 4.3 years with no differences between the two groups. Most women in the sample were recruited during the second trimester (gestational age of 19.4 ± 2.1 weeks). BMI was slightly higher for women with asthma (25.8 ± 3.6 kg/m²) compared to women without asthma (24.9 ± 3.4 kg/m²) but did not reach statistical significance ($p = 0.08$). Overall smoking rates in the sample were low (4.1%) and comparable between the two groups (Table 1).

At recruitment mean FVC% was lower in women with asthma (93.1 ± 8.2) compared with women without asthma (96.4 ± 7.9). Likewise, mean FEV1% was lower in women with asthma (88.9 ± 9.3) compared with women without asthma (94.8 ± 8.7), and the FEV1/FVC ratio was similar between both groups (95.4 ± 4.2 vs 96.1 ± 4.0). Throughout gestation, both groups demonstrated longitudinal changes in lung function, yet the trend over time was different for each group. Non-asthmatic women had a steeper decline in both FVC% and FEV1%, whereas women with asthma had stable FEV1% throughout, and a small improvement in FEV1/FVC ratio (Table 2).

To estimate how lung function changed week by week

Table 1. Baseline characteristics of study participants (N = 460)

Characteristic	Asthmatic women (n = 230)	Non-asthmatic women (n = 230)	p-value
Age, years (mean ± SD)	27.8 ± 4.4	27.4 ± 4.2	0.42
Gestational age at recruitment (weeks)	19.5 ± 2.0	19.3 ± 2.2	0.33
BMI, kg/m² (mean ± SD)	25.8 ± 3.6	24.9 ± 3.4	0.08
Smokers, n (%)	11 (4.8%)	8 (3.5%)	0.48
Parity ≥2, n (%)	118 (51.3%)	122 (53.0%)	0.72

during pregnancy, mixed-effects regression models were fitted for each group while controlling for maternal age, BMI, and smoking. The analysis of the data revealed distinct patterns in both groups. Using FVC%, an indication of total lung capacity, it was seen that women without asthma declined significantly by 0.12% per week. Although women with asthma also declined, the rate of change was significantly slower with a decline of only 0.07% per week. The difference between groups was even larger for FEV1% (airflow), where non-asthmatic women significantly declined by 0.15% per week, while asthmatics exhibited no statistically significant weekly change in FEV1% values. When analyzing the ratio of FEV1/FVC (which calculates the degree of airway obstruction), the non-asthmatic group exhibited no significant change over time and remained within the normal limits of this measure, while women with asthma had a small but statistically significant increase in the weekly ratio. In addition, for all three measures, the rate of change we calculated to be significantly different between groups (Table 3).

Figure 1 illustrates longitudinal changes in forced vital capacity (FVC %) during pregnancy among women with and without asthma. Both groups demonstrated a gradual decline in FVC % as gestation progressed in keeping with the expected extrapulmonary restriction as the uterus grows. However, the magnitude of decline was higher among non-asthmatic women (approx. 0.12 % per week) vs. the asthmatic women (0.07 % per week). While asthmatic women had lower baseline values, they had a relatively milder decrease in FVC % across gestation.

As illustrated in Figure 2, the longitudinal patterns of forced expiratory volume in one second (FEV1%) during pregnancy were markedly different among pregnant

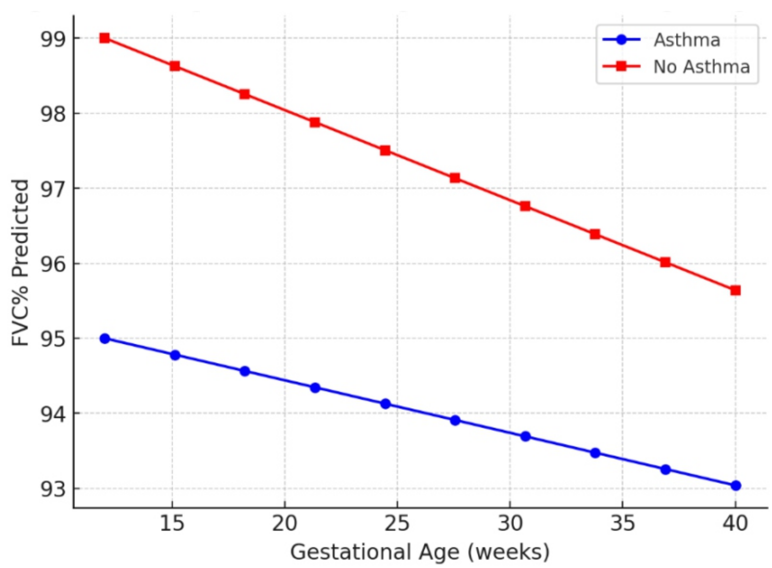

Figure 1. Longitudinal changes in FVC% During Pregnancy

Table 2. Mean spirometric values across pregnancy trimesters

Parameter	Trimester	Asthmatic women (mean ± SD)	Non-asthmatic women (mean ± SD)	p-value
FVC%	1st	94.6 ± 7.9	97.2 ± 7.5	0.02
	2nd	92.8 ± 8.3	95.5 ± 7.6	0.01
	3rd	90.5 ± 8.7	92.1 ± 7.9	0.09
FEV1%	1st	89.5 ± 9.2	95.2 ± 8.5	<0.001
	2nd	88.7 ± 9.1	93.6 ± 8.9	<0.001
	3rd	87.9 ± 9.4	91.1 ± 9.2	0.004
FEV1/FVC ratio	1st	94.9 ± 4.1	95.8 ± 4.2	0.10
	2nd	95.7 ± 4.0	96.0 ± 3.9	0.52
	3rd	96.4 ± 4.3	96.1 ± 4.1	0.60

women with and without asthma. The reductions in FEV1% in non-asthmatic women during pregnancy were clinically and statistically significant. FEV1% statistically declined during the course of gestation by nearly 6% from mid-pregnancy to term on average. Notably, pregnant women with asthma had FEV1% values that appeared relatively stable across pregnancy, with an average decline of only a small and not statistically significant amount. This suggests pregnancy has an impact on lung function; asthma may alter the trajectory of FEV1% and may involve possible effects of active asthma management or medication use.

Figure 3 presents the longitudinal changes in FEV1/FVC during pregnancy. For the non-asthmatics, there was no significant temporal change in the ratio throughout pregnancy, as it exhibited stability at all time points without significant weekly change. The asthmatics did show a change over time in favor of the FEV1/FVC ratio, and while still greatly lower than the non-asthmatics, the ratio increased over time with an increasing proportionality, this reflects that the FEV1 began to stabilize for the asthmatics while the FVC gradually declined, this suggests that

good asthma control throughout pregnancy may help preserve ventililatory performance.

Discussion

In the present study, lung function data were collected on 230 pregnant asthmatic women and 230 pregnant women without asthma. The study produced three main results. First, the estimated change in forced vital capacity (FVC%) was reduced more among women without asthma than women with asthma. Second, the estimated change in forced expiratory volume in one second (FEV1%) fell significantly in women without asthma only; women with asthma sustained stable FEV1% values throughout the study. Third, women with asthma experienced a small yet statistically significant increase in the FEV1/FVC ratio that was not present for women without asthma.

Our observation that FVC% declined more steeply in non-asthmatic pregnant women (–0.12% per week) than in the asthmatic counterparts (–0.07% per week) is consistent with the international longitudinal cohort with women, reported by Jensen et al., where a similar overall trajectory (–0.07% per week) was observed, but with the asthmatic women exhibiting attenuated decline compared to the non-asthmatic women.[11] This lends additional support to the hypothesis that asthma may be protective against gestational restrictive effects, via a maintained airway tone, or through active pharmacological management. In another study from India on uncomplicated pregnancies showed that FVC values decreased significantly when compared to non-pregnant controls. This was due to the diaphragmatic elevation by the gravid uterus and FEV1 fell less than FVC and there was a relative increase in the FEV1/FVC ratio.[12] Although this was not specific to asthmatics, the mechanical principle supports our pattern of declining FVC not being matched by an equal decline in FEV1. Another prospective study involving healthy women by Grindheim et al., showed that FVC and

Table 3. Mixed-effects regression analysis of lung function changes across gestation

Parameter	Group	Weekly change (β) %	95% CI	p-value
FVC%	Non-asthmatic	–0.12	–0.16 to –0.08	<0.001
	Asthmatic	–0.07	–0.11 to –0.03	0.002
	Interaction	—	—	0.03
FEV1%	Non-asthmatic	–0.15	–0.19 to –0.11	<0.001
	Asthmatic	–0.02	–0.06 to +0.02	0.28
	Interaction	—	—	<0.01
FEV1/FVC ratio	Non-asthmatic	+0.01	–0.02 to +0.04	0.55
	Asthmatic	+0.05	+0.01 to +0.09	0.01
	Interaction	—	—	0.04

FVC% actually rose significantly from 14–16 weeks onward, particularly in parous women. This suggests that parity and how people adapted to thoracoabdominal mechanics could play a role in modulating the pattern of declining FVC postpartum.[11] The inconsistencies between their findings and ours may reflect ethno-genre-parity- or health-care related differences between our cohorts.

The relatively unchanged FEV1% in asthmatic women in our cohort (–0.02% per week, non-significant) versus the decline in FEV1% (–0.15% per week) in non-asthmatics is consistent with the more extensive findings in Jensen et al.,[11] whereby the FEV1% in asthmatics was stable and non-asthmatics experienced a decline in FEV1%. This suggests that asthma control regimens may mitigate the decline in expiratory flow, independent of the mechanical

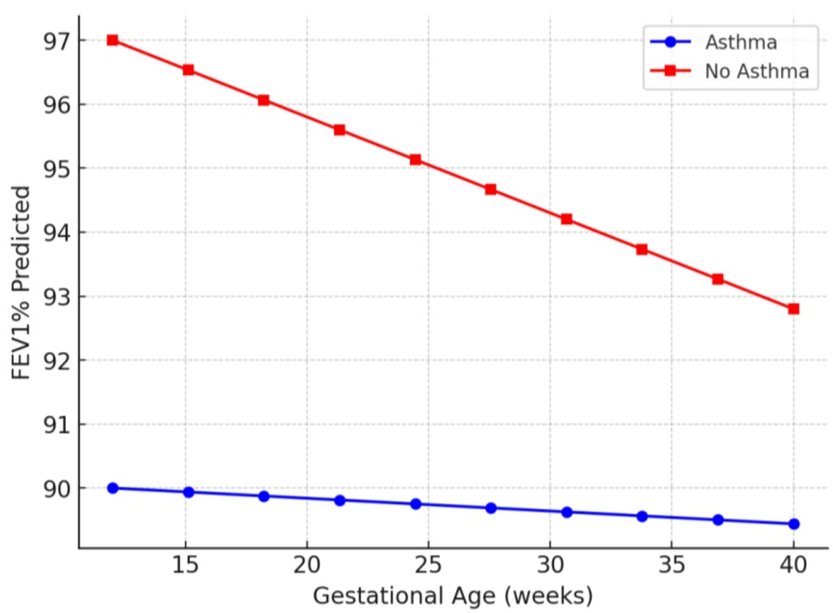

Figure 2. Longitudinal changes in FEV1% during Pregnancy

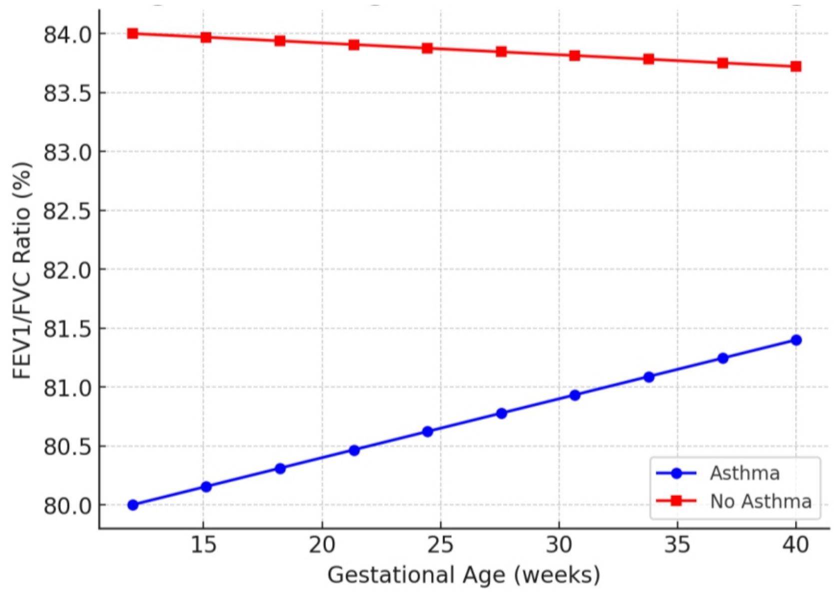

Figure 3. Longitudinal changes in FEV1/FVC Ratio during Pregnancy

perturbations of pregnancy. Earlier, Murphy & Jensen reviewed airway function in pregnancy, and highlighted that while there are small (and usually clinically insignificant) declines in spirometric measures, importantly, there was a lack of data comparing and contrasting the asthma trajectories against non-asthmatics in longitudinal studies.[14] Our study is one of the few to address that gap, documenting the FEV1 decline trajectory for non-asthmatics.

Rohn et al. (2023) examined asthma medication treatment implement and control patterns [+/-] in pregnancy, reporting longitudinal assessments but concluded that symptomatology should be the focus, not spirometric trajectories. Their groups reported dynamic shifts in asthma status with medication implementation and modification, by trimester and over the course of pregnancy, and reasoned that medications consumed in a controlled manner should reduce possible fluctuations in lung function, such as FEV1.[15] Whilst not directly measuring FEV1, the implications from their findings align with our findings.

We found a small but statistically significant increase in FEV1/FVC ratio among asthmatics (+0.05% per week), whilst non-asthmatic women showed no change. This is similar to the Jensen et al. found an increase (~0.06%/week) in asthmatics compared to stability in non-asthmatics,[11] reinforcing asthma management may help prevent expiratory flow from declining in relation to volume, at least as an artefact of lung load.

One cross sectional study from North India also assessed the impact of pregnancy and showed a FEV1/FVC ratio increase occurred as FEV1 declined less than FVC, consistent with the restrictive pattern of pregnancy.[12] And while the study did not assess lung parameters longitudinally nor within an asthma population, it adds some mechanistic rationale for the ratio increase in pregnant lungs but under the load of additional physiology.

The Stevens et al (2022), study also assessed maternal adiposity and found an association between higher, early first trimester BMI and weight gain associates with reduced FEV1/FVC ratio and overall FVC across pregnancy.[16] While I am speculating if the superfluity of factors, such as BMI; might we blunt improvement of these ratios. In our clinical domain, if we had controlled for BMI within our models, we could differentiate the impact of asthma from mechanical influences to more fully explain the clinical relevance.

These implications are important for clinical relevance. First, they contribute to understanding that normal spirometric ranges during pregnancy do vary depending on asthma status, thus clinicians should keep both gestational age and underlying respiratory disease in mind when interpreting FVC and FEV1 trends. Secondly, the sustained FEV1 and the improved FEV1/FVC ratio in asthmatic women suggest that well-controlled asthma during pregnancy may be of some protection for lung function. Finally, this study is particularly important as it provides important regional context, as there are few other studies in South Asia published; our results provide regionally-relevant information to guide obstetric practice in Pakistan and exemplifies the need to incorporate spirometry into routine antenatal assessments in pregnant women with asthma.

This study has several important limitations. First, the absence of postpartum data means we are unable to determine if the observed spirometric trends reverse after delivery; consequently, we cannot parallel findings from studies like the Oslo cohort,[11] which documented a rebound in FVC during the postpartum period. Second, while we noted a potential protective effect of asthma management, our analysis lacked longitudinal details on specific medication regimens. This omission, in contrast to the work of Rohn et al.,[13] limits our ability to conclusively attribute the stability in lung function among asthmatics to treatment effects. Finally, although we adjusted for body mass index, residual confounding from other factors known to influence lung function, such as parity, adiposity distribution, or environmental exposures which remains a possibility, as evidenced by their significant roles in other studies.[6,11]

Conclusion

This longitudinal cohort study of pregnant women in Multan was designed to show an association between advancing gestation and objectively measured changes in lung function, with differences in trajectories between asthmatic and non-asthmatic women. Both asthmatic and non-asthmatic women saw reductions in forced vital capacity % of predicted (FVC%), but the losses were more extensive for non-asthmatics. For forced expiratory volume at one second % predicted (FEV1%), the non-asthmatic women showed statistically significant declines and the asthmatic women were unchanged. Additionally, we noted improvements for FEV1/FVC % predicted in asthmatics and non-asthmatics did not improve. Overall, these findings suggest that pregnancy alters respiratory physiology and there are discrepancies between asthmatics and non-asthmatics that reflect asthma treatment may mitigate decline in function. Clinically, the results of our study suggest that monitoring lung function is important in all pregnant women with careful spirometric assessment because even the non-asthmatic women may have such significant restrictive changes.

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