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Maternal Asthma, Pregnancy, Delivery and Birth Outcomes: A Retrospective Cohort Study

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ABSTRACT

The aim of current study was to determine women´s maternal asthma in pregnancy, delivery and birth outcomes.

Using a retrospective cohort design, data of 580 pregnant women were gathered form a large teaching hospital in Tehran, Iran. The medical records of pregnant women who had attended this hospital between 2009 and 2011 were assessed. Data of delivery and birth outcomes were gathered by observation and medical records of women. Multiple logistic regression and adjusted odds ratio (OR) were used to assess the independent association of asthma and outcomes.

274 patients (47.2%) were in "asthmatic group" and 306 patients (52.8%) were in the "non-asthmatic group". Basic and demographic variables showed the same distribution across two groups. Maternal asthma showed an adjusted relationship with gestational diabetes (OR=2.64), gestational hypertension (OR=3.79), cesarean delivery (OR=2.68), small for gestational age (OR=2.86), premature rupture of membrane (OR=2.18), preterm delivery (OR=1.74), abnormal vaginal bleeding (OR=3.75), and low birth weight (OR=1.78) significantly ($p<0.05$ for all associations).

The majority of pregnancy, delivery and birth outcomes except fetal death, abortion, placenta previa and placenta abruption) were significantly associated with maternal asthma. The largest association of maternal asthma was with gestational hypertension and abnormal vaginal bleeding respectively.

Keywords: Asthma; Birth outcomes; Pregnancy; Pregnancy outcomes

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INTRODUCTION

Asthma is a common chronic non-communicable disease that affects as many as 334 million people of all ages in all parts of the world.[1] This common disease

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could affect women during pregnancy with different complications. Prevalence of asthma during pregnancy has been reported with a wide range from 3.4% to 12.4%.[2] This disease was known as the most common chronic problem during pregnancy.[3] In a survey from Iran, prevalence of asthma among pregnant women with dyspnea was reported 38.8%.[4] However, there is not a valid estimate of asthma among adults and during pregnancy in Iran. While the prevalence of asthma in children under the age of 18 years was reported about 35% in Tehran, and 13% in Iran using a systematic review.[5]

There are several studies in which asthma was considered as a risk for mother and fetus during pregnancy. Specially this risk is higher in women with poorly-controlled asthma.[6,7] The most common complications of asthma during pregnancy included low birth weight, preterm birth, small for gestational age (SGA), and preeclampsia.[8] These reports are mostly from population-based studies. It is challenged that, in hospital-based studies the relationship between asthma, maternal and fetal morbidities are weaker and sometimes insignificant.[9] The reason could be explained by the low power and sample size of hospital-based studies. Therefore, the aim of current study was to determine the outcomes of pregnancy, delivery and fetal of maternal asthma using a retrospective cohort design in Tehran, Iran.

MATERIALS AND METHODS

Study Participants and Setting

This study was conducted in Akbarabadi Hospital which is a large, teaching gynecology central hospital in Tehran, the capital of Iran. As a retrospective cohort study we gathered our data from hospital records of pregnant women admitted to prenatal clinic between 2009 and 2012. The inclusion criteria included medical records of pregnant women aged between 18 to 50 years old admitted to hospital to get prenatal care. We used a convenient sampling method to select the medical records. In order to get 15% difference in low birth weight between asthmatic and non-asthmatic pregnant women (assuming 10% in non-asthmatic and 25% in asthmatic groups),[10] with power of 80% and type one error of 5% and considering 20% for missing data, our sample size was estimated to be at least 270 per group. If a patient had at least one prescription of asthma medications and diagnosis of asthma two years before pregnancy and through pregnancy, we enrolled her in exposed group; if not she was considered as a control (unexposed). Outcome data (related to delivery and fetal) was collected by both medical records and interview with mothers. Informed consent was taken from mothers to participate in the study. The ethics committee of Iran University of Medical Sciences approved the study (No. IR.IUMS.REC.1392-22659).

Data Collection and Measures

To collect data we filled out a form for each patient in both groups, which included data on maternal characteristics such as age, education level, smoking history, pregnancy variables such as gestational diabetes, gestational hypertension, type of asthma medication intake, gestational age, and maternal diseases such as chronic diabetes and hypertension. We also gathered data on delivery outcomes such as neonatal gender, low birth weight, SGA, neonatal birth weight, premature delivery (which is defined as delivery before 37 weeks of gestation), caesarian section, fetal mortality, placenta abruption, placenta previa, Apgar, bleeding before and through delivery and premature rupture of membrane (PROM).

Gestational diabetes was defined as a condition when two of four glucose levels of the oral glucose tolerance test (OGTT) met or exceeded the upper limits of normal. Chronic diabetes was defined as a diabetes which is diagnosed before 20 weeks of gestation. We defined gestational hypertension as the elevation of blood pressure during the second half of pregnancy including eclampsia, preeclampsia and transient hypertension. Chronic hypertension was defined as having hypertension before pregnancy or before 20 weeks of gestation. Fetal mortality was defined as loss of pregnancy product after 20 weeks of gestation. Placenta abruption was considered as a condition when some parts of placenta separate from the uterus prematurely. Placenta previa was also defined as a condition when placenta locates near or over the internal os of the cervix, and PROM was defined as rupture of membrane at any time before the onset of contractions.[11]

Data Analysis

Data were analyzed using SPSS version 21.0.1 (SPSS Inc., Chicago, IL, USA). We used frequency tables to present qualitative variables. Mean, median and standard deviation were used to summarize numeric variables. We used t-test and chi-square for

comparing categorical variables between two groups. Man-Whitney U-test was used for comparing first minute and fifth minute Apgar score across two groups. Logistic regression models were used to find the independent association of maternal asthma on pregnancy, delivery and birth outcomes. We put each found variable as a risk factor of pregnancy and delivery outcomes in bivariate analysis with *p* Value of less than 0.05. The fit of the data in every model was assessed with the Hosmer-Lemeshow test of goodness-of-fit and the generalized R-square measure. Crude and adjusted odds ratio were calculated for each outcome with 95% confidence interval. We considered level of significance at 0.05.

Table 1. Demographic and medical characteristics of asthmatic pregnant women, Akbar-Abadi hospital, Tehran, Iran (n=580)

	Pregnant women with asthma n=274 Number (%)	**Pregnant women without asthma n=306 Number (%)**	***p*-value**
Education level			0.34
Illiterate & primary	181 (70.2)	189 (65.2)	
Secondary & high school	71 (27.5)	96 (33.1)	
High school graduated	6 (2.3)	5 (1.7)	
Smoker			0.40
Yes	17 (6.2)	24 (7.8)	
No	257 (93.8)	282 (92.2)	
Chronic diabetes mellitus			0.30
Yes	11 (4)	8 (2.6)	
No	263 (96)	298 (97.4)	
Chronic hypertension			0.17
Yes	13 (4.7)	8 (2.6)	
No	261 (95.3)	298 (97.4)	
Gestational diabetes mellitus			0.003
Yes	37 (13.5)	19 (6.2)	
No	237 (86.5)	287 (93.8)	
Gestational hypertension			0.0001
Yes	50 (18.2)	17 (5.6)	
No	224 (81.8)	289 (94.4)	
Abnormal vaginal bleeding[*]			0.0001
Yes	25 (9.7)	7 (2.4)	
No	234 (90.3)	281 (97.6)	
Fetal mortality[*]			0.009
Yes	22 (8.5)	9 (3.1)	
No	237 (91.5)	279 (96.9)	
Preterm delivery[*]			0.0001
Yes	80 (33.6)	54 (19.1)	
No	158 (66.4)	229 (80.9)	
Premature rupture of membrane			0.001
Yes	59 (22.8)	35 (21.1)	
No	200 (77.2)	254 (87.9)	
Cesarean section[*]			0.0001
Yes	141 (54.4)	101 (35.1)	
No	118 (45.6)	187 (64.9)	
Low birth weight[*]			0.001
Yes	53 (22.3)	32 (11.3)	
No	185 (77.7)	251 (88.7)	
Small for gestational age[*]			0.0001
Yes	47 (19.7)	19 (6.7)	
No	192 (80.3)	265 (93.3)	

*There were some missing data, because we excluded pregnancies with abortion from some maternal and birth outcomes.

RESULTS

This retrospective cohort study included 580 pregnant women admitted to prenatal clinic of Akbarabadi hospital for prenatal care. 274 patients (47.2%) in asthmatic group and 306 patients (52.8%) were in non-asthmatic group. In the asthmatic group, 174 patients (63%) used inhaled Salbutamol, 54 patients (20%) used inhaled corticosteroid and 26 patients (10%) used oral corticosteroids. 20 patients (7%) did not use any medication despite having asthma diagnosis. The mean age in asthmatic and non-asthmatic women were 28.5±5.7 and 29.1±6 years, respectively (p= 0.18). As shown in Table 1, there was no significant difference in education level and smoking history in two groups as baseline characteristics. Also there was no significant difference in diabetes mellitus and hypertension between asthmatic and non-asthmatic pregnant women.

There was a significant difference in gestational diabetes mellitus, gestational hypertension, abnormal vaginal bleeding, fetal mortality and preterm delivery across two groups. We also found a significant difference regarding PROM and cesarean section (CS) between two groups (p<0.05). Low birth weight was 2.2 times more in asthmatic pregnant women than non-asthmatic ones (p=0.001), and having SGA was 3.4 times more in exposed than control group (p=0.0001) (Table 1).

There was a significant difference for neonatal birth weight in asthmatic and non-asthmatic women (2821.3±891.7 versus 3014±603 respectively, p=0.003). The first-minute Apgar score in non-asthmatic group was statistically higher than asthmatic group (8.02 and 8.60, respectively; p=0.04). Apgar score was almost identical for fifth minute between two groups (9.06 versus 9.69, p=0.001).

In contrast, we did not find any significant difference in incidence of placenta previa and placenta abruption between asthmatic and non-asthmatic pregnant women (p=0.26 and p=0.1, respectively). There was not also any significant difference regarding abortion between two groups. (p=0.8)

The results of logistic regression for outcomes with significant difference between two groups and the crude odds ratio for these outcomes are shown in Table 2. With the exception for fetal mortality which did not remain significant after adjustment for PROM and age, other fetal and maternal outcomes (gestational diabetes mellitus, abnormal vaginal bleeding, preterm delivery, PROM, CS, low birth weight and being SGA) remained statistically significant after adjusting for important covariates. Gestational diabetes mellitus, PROM, CS and being SGA increased more than two times in mothers with asthma. Vaginal bleeding was more than three times common in mothers with asthma with a statistically significant difference.

Table 2. Crude and adjusted odds ratios (OR) of maternal asthma as risk factor of pregnancy, delivery and birth outcomes with 95% confidence interval (CI)

Maternal and birth outcomes	Crude		Adjusted	
	OR	CI	OR	CI
Gestational diabetes mellitus [1]	2.35	1.32- 4.20	2.64	1.45- 4.78
Gestational hypertension	3.79	2.13- 6.75	3.79	2.10- 6.70
Abnormal vaginal bleeding [2]	4.28	1.82- 10.09	3.75	1.54- 9.10
Fetal death [3]	2.87	1.30- 6.37	1.53	0.57- 4.12
Preterm delivery [4]	2.14	1.43- 3.20	1.74	1.14- 2.65
Premature rupture of membrane[5]	2.14	1.35- 3.38	2.17	1.36- 3.47
Cesarean section [6]	2.21	1.56- 3.12	2.08	1.43- 3.02
Low birth weight [7]	2.24	1.39- 3.62	1.78	1.07- 2.94
Being small for gestational age [8]	3.41	1.94- 6.00	2.86	1.46- 5.60

1. OR adjusted for age
2. OR adjusted for education, gestational diabetes and gestational age.
3. OR adjusted for PROM and gestational age.
4. OR adjusted for gestational hypertension, abnormal vaginal bleeding, PROM and age.
5. OR adjusted for preterm delivery.
6. OR adjusted for gestational hypertension, preterm delivery, low birth weight, small for gestational age and PROM.
7. OR adjusted for abnormal vaginal bleeding and gestational hypertension.
8. OR adjusted for gestational hypertension, preterm delivery and low birth weight.

DISCUSSION

In this retrospective cohort study, we studied 274 asthmatic pregnant women as exposed group and 306 non-asthmatic pregnant women as control group. We found significant differences in maternal outcomes such as gestational diabetes mellitus, gestational hypertension and abnormal vaginal bleeding in asthmatic pregnant women compared to non-asthmatic pregnant women. In studies by Ivancso et al.[12] and Schatz et al.[13] increased incidence of preeclampsia in asthmatic women was reported. In a meta-analysis of cohort studies, preeclampsia was reported with relative risk of 1.54 in asthmatic pregnant women. This study also reported an increase in some other birth outcomes such as low birth weight (LBW), SGA and preterm delivery.[8] These finding are similar with our study.

In another study which was conducted in Iran, Karimi et al.[10] found a significant association between maternal asthma and birth outcomes such as prematurity, LBW and CS. In a prospective cohort study the authors did not report any significant difference in preterm delivery and also maternal complications such as gestational diabetes mellitus, preeclampsia and PROM between asthmatic pregnant women and control group. In this study the only outcome with significant difference between two groups was CS, which was 1.4 times higher in asthmatic women.[14]

In our study after adjustment for some important covariates, preterm delivery, LBW, and CS were more common in asthmatic than control group. We also found gestational diabetes and PROM more common up to two times in exposed than non-exposed group. In our study gestational hypertension occurred 3.79 times more in asthmatic women. Our results confirm previous studies which reported increased preterm delivery,[8,9,14] LBW,[8,10] CS,[10,14,15] PROM,[16] gestational diabetes[16] and hypertension.[8,12,13,15,16]

In a similar retrospective cohort study in the Canadian province of Quebec, Liu et al. reported statistically significant association between asthma and some maternal and fetal adverse outcomes such as preterm delivery, gestational hypertension, placenta abruption and CS.[9] These findings were similar to our results except for placenta abruption that was not significant in the current study. Wen et al. reported statistically significant increase in placenta abruption in asthmatic women even after adjustment for maternal age, gestational diabetes, pre-existing diabetes, and pre-existing hypertension.[16]

Some fetal and maternal outcomes in asthmatic pregnant women could be explained by the effect of oxygen deprivation and hypoxia on fetal growth in long term.[7,17,18] As reported by Firoozi et al.[7] and Bracken et al.,[18] severe and moderate asthma increase the risk of SGA in comparison to mild asthma. Some other fetal and maternal outcomes could be accounted for by the effect of asthma medications during pregnancy too. Bracken et al.[18] in a prospective study on symptoms, severity and treatment in asthma concluded that asthma symptoms or severity have no effect on preterm delivery and it is the medications especially oral steroid and theophylline which are the reason of preterm delivery.

In a historical cohort study on 2,017,553 deliveries in Canada, the adverse effect of asthma on some fetal and maternal outcomes such as preterm delivery, gestational hypertension, gestational diabetes, antepartum and postpartum hemorrhage, PROM and CS, after adjustment for important confounding factors using multiple logistic regression analysis, was reported.[16] These results are in accordance with our study. One other study also reported higher incidence of abnormal vaginal bleeding in asthmatic pregnant women.[15]

The crude odds ratio for fetal death in current study was 2.87 (95% CI 1.30- 6.37). After adjustment for PROM and age, the adjusted odds ratio was 1.53 (95% CI 0.57- 4.12), which was not statistically significant any more. The same as our study, Breton et al. in a cohort study reported statistically significant increase of 34% in fetal death among asthmatic women compared to non-asthmatic women. After adjustment for placental abruption and smoking, this difference did not remain significant (OR 1.12, 95% CI 0.87-1.45).[19] Some other studies reported same findings.[14,20] In these studies the association of asthma with fetal mortality became non-significant after adjustment for important confounding factors. In contrast an increase in infant death was reported in a study by Kallen et al on Swedish deliveries.[21]

We did not find any statistically significant relationship between asthma and abortion and placenta previa. In the study of Dombrowski et al. the risk of previous abortion in severe, moderate and mild asthma was not higher than control group.[14] While, Karimi et al.[10] and Tata et al.[22] reported slightly increased risk of

abortion in asthmatic pregnant women. Wen et al. in their study on 2,017,553 deliveries, reported increased risk of placenta previa before and after adjustment of maternal age and previous CS.[16] These different results could be due to different population and sample size of studies and need more investigations.

As a limitation of current study, we did not collect data on women's body mass index which may be a confounding factor. Also, the level of asthma control, exacerbation or hospitalization during pregnancy may have effect on maternal and birth outcomes that were not considered in current study. The other limitation was using medical records to collect part of data. The reliability and validity of such data should be considered by caution. Also, some records did not have complete and enough data to use in current study. Finally, we used a convenient sample which may not have been representative of all asthmatic pregnant women.

In conclusion, we found the association of asthma with some important maternal and birth outcomes such as gestational diabetes, gestational hypertension, CS, SGA, PROM, preterm delivery, abnormal vaginal bleeding and LBW; which shows the importance of controlling asthma in pregnant women and maybe integrating the asthma care in routine prenatal care.

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