

Maternal and Neonatal Complications of Asthma, a Study in Iran

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Article Info

 [10.30699/jogcr.6.2.65](https://doi.org/10.30699/jogcr.6.2.65)

Received: 2020/11/22;

Accepted: 2021/02/10;

Published Online: 5 Mar 2021;

Use your device to scan and read the article online



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ABSTRACT

Background & Objective: Asthma is the most common chronic respiratory disorder during pregnancy and it may affect pregnancy outcomes. This study aims to compare the pregnancy, delivery and neonatal outcomes between asthmatic and non-asthmatic pregnant women.

Materials & Methods: The study was designed as a historical cohort among pregnant women with and without asthma. A total number of 583 asthmatic patients were allocated to the case group and 753 women without asthmatic history were placed in the control group. Pregnancy, labor and neonatal outcomes were compared between the two groups.

Results: The baseline characteristics of the women in both groups did not show significant differences. Gestational hypertension was more in the asthmatic group [43 (7.37%) VS 26 (3.45%), $P=0.001$]. Also, the rate of preterm delivery was higher in asthmatic women (72 (12.34%) VS 77 (10.22%) in the control group, $P=0.04$). However, the rate of preeclampsia was less in the asthmatic group [29 (4.97%) VS 71 (9.42%), $P=0.008$]. Apgar score at minutes 1 and 5 was less in asthmatic group. Intra Uterine Fetal Demise (IUFD) (24 (4.1%) VS 13(1.7%), P value=0.009), and neonatal death (31 (5.31%) VS 10 (1.32%), $P=0.001$) were more in the asthmatic group. The maternal and neonatal complications did not show significant differences in various severities of asthma. Multivariate regression model showed more risks for neonatal death (adjusted odds ratio (AOR)=4.18; CI95% 2.03-8.60), IUFD (AOR=2.43; CI95% 1.22-4.82), gestational hypertension (AOR= 1.43; CI 95% 1.40-1.45), and lower risk for preeclampsia (AOR 0.37; CI95%0.17-0.79) in asthmatic women.

Conclusion: Regardless of the fact that asthmatic mothers had higher frequencies of gestational hypertension, IUFD and neonatal death, the effect of asthma on perinatal outcome is minimal, probably because of efficient medical control.

Keywords: Asthma, Gestational hypertension, Intrauterine fetal demise (IUFD), Neonatal death, Neonate, Preeclampsia, Pregnancy



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Introduction

Asthma is the most common chronic respiratory disorder during pregnancy with a prevalence up to 12% in childbearing age and therefore, it may affect pregnancy outcomes (1, 2). Its incidence is under the influence of smoking, genetics and environmental factors (3, 4). The frequency of asthma among Iranian population has been reported around 7.6 to 8.9% which is similar to Asian and European countries (5, 6). Higher frequency of pregnancy complications was previously addressed among women with asthma by some studies (7, 8). Furthermore, asthma's prevalence among pregnant women has increased recently (9).

Prematurity, low birth weight and congenital abnormalities were among reported complications of babies born from asthmatic mothers (10, 11, 12). There are also some adverse neonatal outcomes including respiratory complications, icterus, and neonatal intensive care unit (NICU) admission (13-18). The most attributed reason is respiratory compromise during asthma attacks (12). Also, asthma has been reported to increase the frequency of some complications during pregnancy including gestational diabetes mellitus, intrauterine growth restriction (IUGR), hypertensive disorders, preterm birth and premature rupture of membranes, cesarean deliveries, placental abruption and placenta previa.

The incidence of different complications and their associations with asthma among Iranian mothers and newborns were reported in different frequencies by some studies (13, 17). In the current study, the aim was to find out the frequency of pregnancy, delivery, and newborn complications among asthmatic and non-asthmatic women in three main referral training hospitals in Tehran, Iran.

Materials and Methods

The current study was conducted in Iran University of Medical Sciences (IUMS) and was granted ethics approval. The asthmatic women's data was extracted from registries of referral university hospitals. Consent was obtained from all participants.

A historical cohort study was performed on the patient records of confirmed asthmatic pregnant women who delivered between March 2011 to January 2019 in three training hospitals (Akbarabadi, Firoozgar and Rasoul Akram) affiliated to IUMS and all had complete hospital records with the confirmed diagnosis of asthma. Asthma and its severity was defined by the criteria of Guidelines for the Diagnosis and Management of Asthma (EPR-3) (18) which had been recorded in the patients' records. For each asthmatic patient, one participant without any asthmatic history who delivered at the same period of time was recruited. Inclusion criteria were pregnant women who have developed adult asthma after the age of 15, had a confirmed diagnosis of asthma by a pulmonologist and used medication for at least two years before their pregnancy. The women with any history of other medical disorders were excluded. Also patients' documents with missing data were excluded from the study. Pregnancy complications and related delivery problems recorded by obstetricians in patients' records were evaluated. The neonates had a complete physical examination by a neonatologist until they were discharged from the hospital where their data was extracted from data sheets. Finally, data from 753 women in the control group and 583 asthmatic women in the case group were compared. Demographic data including age, body mass index (BMI), nationality, gestational age, history of smoking or drug abuse and asthma severity were taken into consideration. Asthma severity was assessed regarding patients' medications and available history by the same pulmonologist.

Outcomes including gestational hypertension, premature rupture of membrane (PROM), preeclampsia, eclampsia and severe preeclampsia, abnormal bleeding during each trimester of pregnancy and delivery, routes of delivery, duration of hospitalization in ward or intensive care unit (ICU) for both mothers and newborns, were evaluated and compared in both groups.

Neonatal complications including prematurity, small for gestational age (SGA), intrauterine fetal death (IUFD), neonatal respiratory distress syndrome (RDS), newborn death, intrauterine growth retardation (IUGR), asphyxia, icterus, shoulder dystocia and Apgar score at birth and the fifth minute of birth, were assessed.

SPSS 20 (SPSS Inc., Chicago, IL., USA) was used to compare the data. Chi square test, independent sample t test, binary and multivariate logistic regression were used for data analysis. P-values less than 0.05 were considered significant.

Results

A total number of 583 asthmatic pregnant women (case group) were compared with 753 non-asthmatic patients (control group). A number of 485 (83.9%) asthmatic women used inhaler and 81 (13.9%) consumed both oral medication and inhaler. The baseline characteristics of the women in two groups did not show significant differences (table 1). Gestational hypertension was more in the asthmatic group (43 (7.37%) VS 26 (3.45%), $P=0.001$). Also, the rate of preterm delivery was higher in asthmatic women (72 (12.34%) VS 77 (10.22%) in control group, $P=0.04$). However, the rate of preeclampsia was less in the asthmatic group (29 (4.97%) VS 71 (9.42%), $P=0.008$) (Table 2). Apgar score at minutes 1 and 5 was less in the asthmatic group (Table 3). IUFD (24 (4.1%) VS 13 (1.7%), $P=0.009$), and neonatal death (31 (5.31%) VS 10 (1.32%), $P=0.001$) were more in the asthmatic group (Table 3). Duration of hospital stay was longer both for mothers and babies in the case group (Table 2 and 3). The maternal and neonatal complications did not show significant differences in various severities of asthma (Table 4).

Table 1. Baseline Characteristics of the two groups

| Characteristics | Asthmatics n= 583 | Non asthmatics n= 753 | P-value |
|-----------------|----------------------|--------------------------|---------|
| Age (year) M±SD | 29.66±5.75 | 29.3±5.73 | 0.251 |
| BMI | 28.32±3.78 | 28.11±1.39 | 0.269 |
| Nationality | Iranian | | |
| | 523(89.7%) | 676(89.8%) | 0.501 |

| Characteristics | | Asthmatics n= 583 | Non asthmatics n= 753 | P-value |
|--------------------|---------|----------------------|--------------------------|---------|
| | Afghans | 60(10.3%) | 77(10.2%) | |
| Smoking | | 22(3.8%) | 24(3.2%) | 0.113 |
| Multiple pregnancy | | 27 (4.6%) | 25 (3.3%) | 0.061 |
| Neonatal gender | Female | 301(51.62%) | 386(51.26%) | 0.127 |
| | Male | 282(48.37%) | 367(48.73%) | |

Table 2: Maternal complications in two groups

| Characteristics | Asthmatics n= 583 | Non asthmatics n= 753 | P value |
|-----------------------------------|----------------------|--------------------------|---------|
| Gestational hypertension | 43 (7.37%) | 26(3.45%) | 0.001* |
| PROM | 91(15.60%) | 116(15.40%) | 0.60 |
| Preterm delivery | 72(12.34%) | 77(10.22%) | 0.04* |
| GDM | 52(8.9%) | 63(8.4%) | 0.73 |
| Placental abruption | 25(4.3%) | 32(4.2%) | 0.98 |
| Abnormal bleeding after delivery | 5(0.9%) | 6(0.8%) | 0.90 |
| Abnormal bleeding during delivery | 1(0.2%) | 2(0.3%) | 0.71 |
| First trimester bleeding | 4(0.7%) | 2(0.3%) | 0.25 |
| Second trimester bleeding | 3(0.5%) | 4(0.5%) | 0.96 |
| Third trimester bleeding | 27(4.6%) | 29(3.9%) | 0.48 |
| Eclampsia | 2(0.3%) | 8(1.1%) | 0.12 |
| Sever preeclampsia | 18(3.1%) | 33(4.4%) | 0.21 |
| Preeclampsia | 29(4.97%) | 71(9.42%) | 0.008* |
| Cesarean section | 278(48.6%) | 392(52.1%) | 0.12 |
| Emergency cesarean section | 54(9.4%) | 62(8.2%) | 0.5 |
| Hospitalization (ward) | 2.59±2.76 | 2.49±1.96 | 0.02* |
| Hospitalization (ICU) | 0.22±1.01 | 0.13±0.52 | 0.001* |

*: Significant

Table 3. Neonatal complications in two groups

| Characteristics | Asthmatics n= 583 | Non asthmatics n= 753 | P-value |
|-----------------------|----------------------|--------------------------|---------|
| IUGR | 19(3.3%) | 13(1.7%) | 0.071 |
| SGA | 3(0.5%) | 5(0.7%) | 0.722 |
| Neonatal birth weight | 3251±347 | 3345±148 | 0.287 |
| Shoulder dystocia | 5(0.85%) | 8(1.06%) | 0.732 |
| Apgar minute 1 | 8.02±4.86 | 8.55±1.59 | 0.001* |

| Characteristics | Asthmatics n= 583 | Non asthmatics n= 753 | P-value |
|-----------------------|----------------------|--------------------------|---------|
| Apgar minute 5 | 8.67±3 | 10.08±6.94 | 0.002* |
| IUFD | 24 (4.1%) | 13(1.7%) | 0.009* |
| Neonatal Death | 31(5.31%) | 10(1.32%) | 0.001* |
| RDS | 5(0.9%) | 9(1.2%) | 0.54 |
| Icterus | 16(2.7%) | 26(3.5%) | 0.45 |
| Asphyxia | 5(0.9%) | 4(0.5%) | 0.47 |
| Hospitalization(ward) | 1.41±1.97 | 1.41±1.85 | 0.35 |
| Hospitalization(NICU) | 1.80±5.01 | 1.74±4.86 | 0.91 |

*: Significant

Table 4: The maternal and neonatal complications in different severities of asthma

| Characteristics | Mild asthma | Moderate asthma | Severe asthma | P value |
|-----------------------------------|-------------|--------------------|---------------|---------|
| IUGR | 8 | 9 | 2 | 0.68 |
| PROM | 37 | 37 | 17 | 0.24 |
| Preterm delivery | 73 | 32 | 17 | 0.65 |
| GDM | 25 | 20 | 7 | 0.84 |
| Placental abruption | 16 | 4 | 5 | 0.25 |
| Abnormal bleeding after delivery | 3 | 0 | 2 | 0.26 |
| Abnormal bleeding during delivery | 0 | 0 | 1 | 0.12 |
| bleeding during trimester 1 | 2 | 0 | 2 | 0.19 |
| bleeding during trimester 2 | 1 | 1 | 1 | 0.83 |
| bleeding during trimester 3 | 11 | 11 | 5 | 0.76 |
| Eclampsia | 1 | 0 | 1 | 0.49 |
| Severe pre-eclampsia | 10 | 4 | 4 | 0.65 |
| pre-eclampsia | 10 | 6 | 13 | 0.30 |
| Gestational hypertension | 15 | 13 | 15 | 0.61 |
| IUGR | 8 | 9 | 2 | 0.687 |
| IUFD | 13 | 6 | 5 | 0.70 |
| Neonatal death | 14 | 10 | 7 | 0.78 |
| RDS | 3 | 2 | 0 | 0.82 |
| SGA | 1 | 0 | 2 | 0.85 |
| Icterus | 8 | 5 | 3 | 0.99 |
| Asphyxia | 1 | 3 | 1 | 0.38 |

Multivariate regression model showed more risks for neonatal death (aOR=4.18; CI95% 2.03-8.60), IUFD (aOR=2.43; CI95% 1.22-4.82), gestational

hypertension (aOR=1.43; CI 95% 1.40-1.45), and lower risk for preeclampsia (aOR 0.37; CI 95%, 0.17-0.79), in asthmatic women ([Table 5](#)).

Table 5. Regression model for confounding variables on significant results

| | Gestational hypertension | Preeclampsia | Newborn death | IUFD |
|---|--------------------------|--------------|---------------|--------|
| Nagelkerke R ² /Cox and Snell R ² | 0.22 | 0.14 | 0.18 | 0.17 |
| P-value of the model | 0.001 | 0.001 | <0.001 | 0.001 |
| P-value of the variable between groups | <0.001 | 0.005 | <0.001 | <0.001 |

Discussion

In this study, asthmatic mothers had higher frequency of gestational hypertension, IUFD and neonatal death, however, preeclampsia was lower in mothers with asthma. The other outcomes did not show significant differences between asthmatic and non-asthmatic mothers. The severity of asthma, did not show significant effects on the outcomes. Therefore, irrespective of influential effects of asthma on pregnancy outcomes, its effects are minimal, which is in accordance with a study by Ali *et al.* (20). It may reflect the effects of good medical control of asthma during pregnancy which can reduce the effects of asthma on pregnancy outcomes (10, 21). None of the demographic data including ethnicity showed significant difference. Also, the women with underlying medical disorders were excluded from the study in order to remove the potential confounding factors. Surprisingly, asthma showed a protective effect on preeclampsia. This finding is in contrast with previous studies (8, 10, 16, 22). The protective effects of smoking on preeclampsia has been proposed in the past (23), and hypoxia is a common point in these two different conditions. However, the effects of smoking and asthma on placenta, cardiovascular and immune systems could be the potential reasons. At the same time, genetics and ethnicity might be involved and need more investigations. We did not find significant differences in other complications in women with asthma.

Gestational hypertension was significantly more in mothers with asthma in the present study. In a study by Baghlaf *et al.* (22) greater risk of gestational hypertension, preeclampsia, gestational diabetes mellitus (GDM), placenta abruption, cesarean delivery and postpartum hemorrhage were reported in asthmatic women. Vaezi *et al.* (17), reported a higher frequency of pregnancy complications in Iranian asthmatic mothers, including gestational hypertension, abnormal bleeding, SGA, GDM, PROM, preterm delivery, cesarean delivery and maternal asthma. However, increased risk of fetal death, abortion, placenta previa and placenta abruption were not reported in maternal asthma. Similar results have been reported in other studies (8, 10, 16, 20).

Newborn complications were also assessed in the present study. IUFD and fetal death were significantly higher in asthmatic mothers, unlike other neonatal problems, which is in accordance with the study by Fazel *et al.* (13) and in contrast with another study (19). Apgar

score was less in asthma group in the present study. This finding is in contrast with the study by Fazel *et al.* (13) that reported no relationship between Apgar score and maternal asthma.

Furthermore, in a study in Finland (24), perinatal mortality, preterm birth, low birth weight, SGA, and asphyxia were higher among asthmatic mothers. In another study in Norway, preterm birth was highly associated with maternal asthma (25).

Some studies did not confirm the relationship between severity of asthma and maternal or neonatal problems (7, 15), which is in accordance with the present study, however, it is in contrast with another study (8).

It is recommended to perform further studies in order to find the incidence of different perinatal complications in asthmatic mothers with different severities, different medications and various routes of administration and dosages.

Conclusion

Regardless of the fact that asthmatic mothers had higher frequencies of gestational hypertension, IUFD and neonatal death, the effect of asthma on perinatal outcome is minimal, probably because of efficient medical control.

Conflict of Interest

Authors declared no conflict of interests.

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How to Cite This Article:

Kashanian M, HoseiniMoghaddam A, Javad Moosavi S A, Sheikhsari N, Abdollahi H. Maternal and Neonatal Complications of Asthma, a Study in Iran. *J Obstet Gynecol Cancer Res.* 2021; 6 (2) :65-71

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